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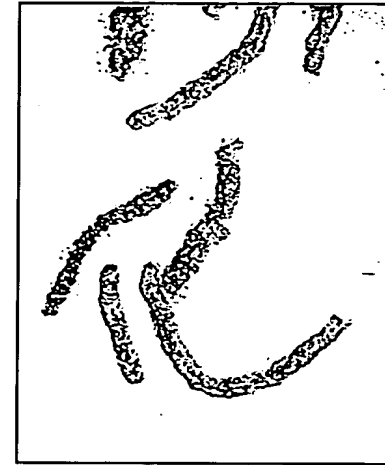
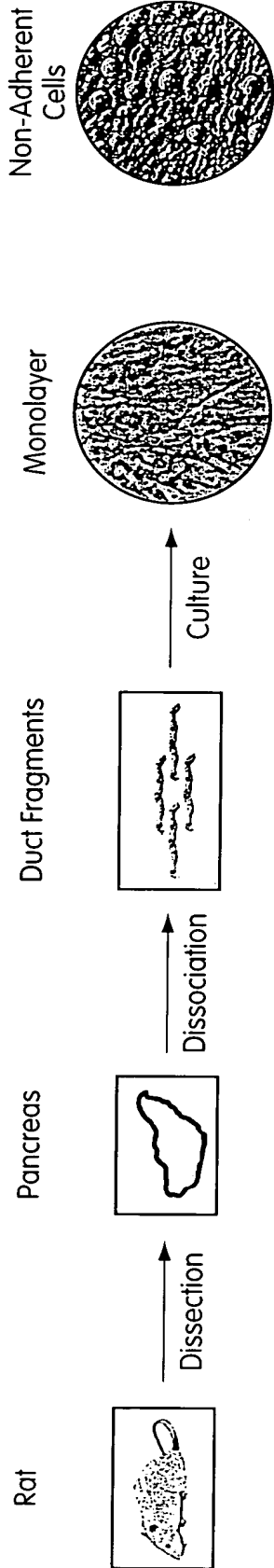
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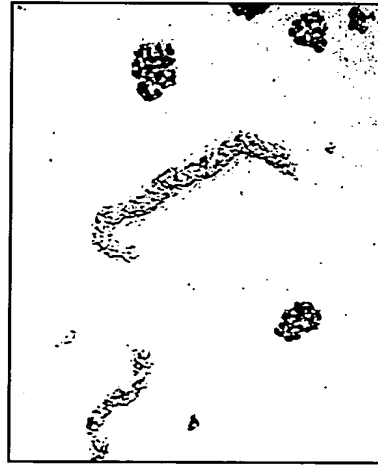
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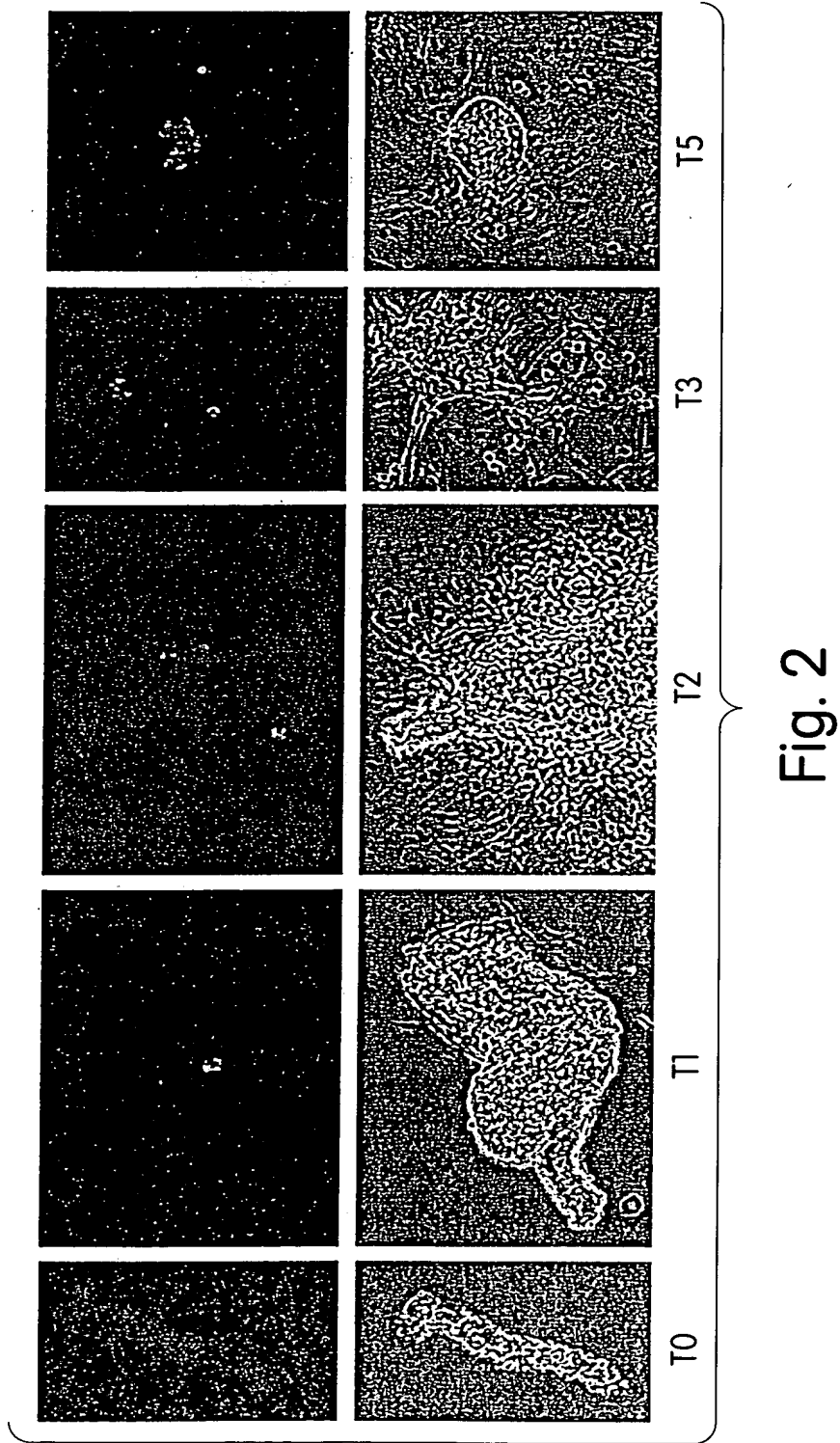


Primary Digest

Fig. 1



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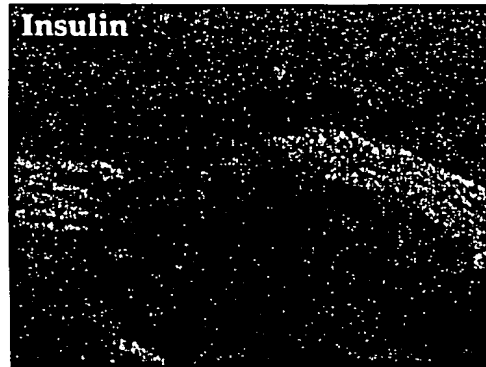


Fig. 3A

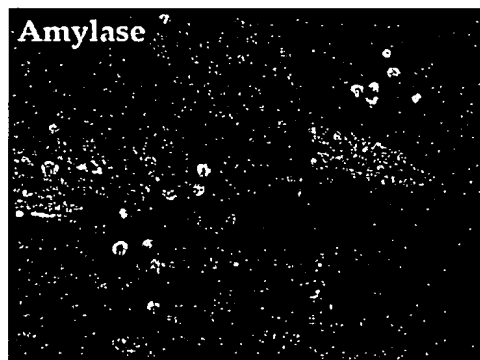


Fig. 3B

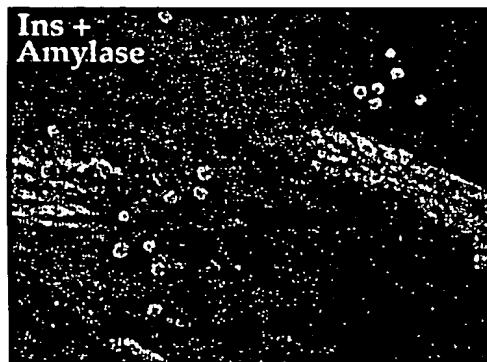


Fig. 3C



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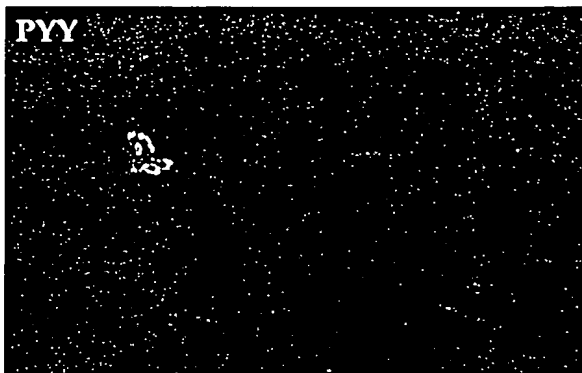


Fig. 3D

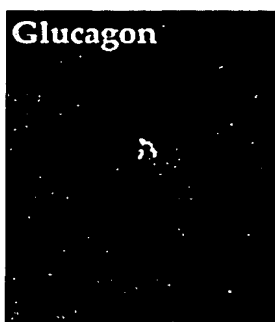


Fig. 3E

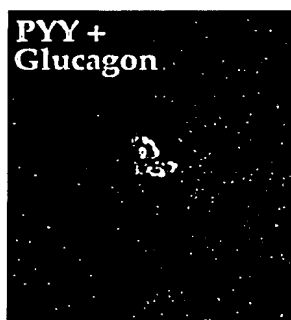


Fig. 3F

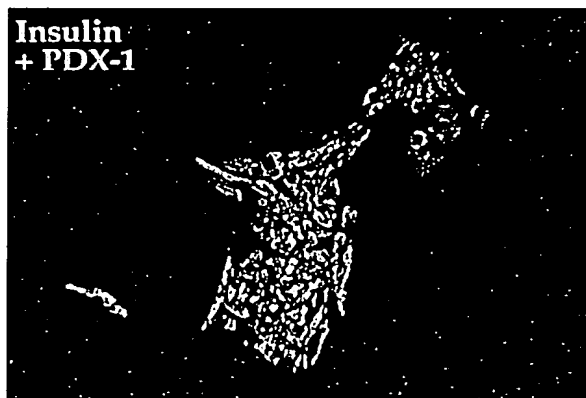


Fig. 3G



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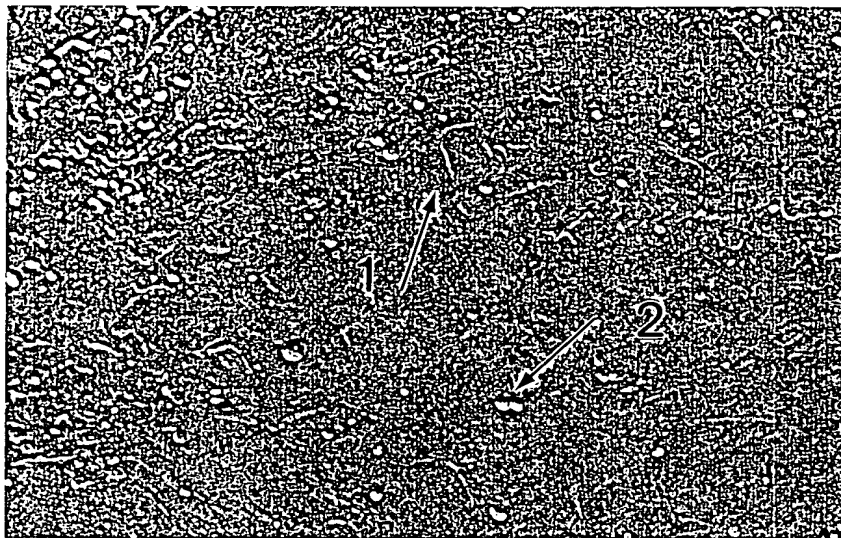


Fig. 4A

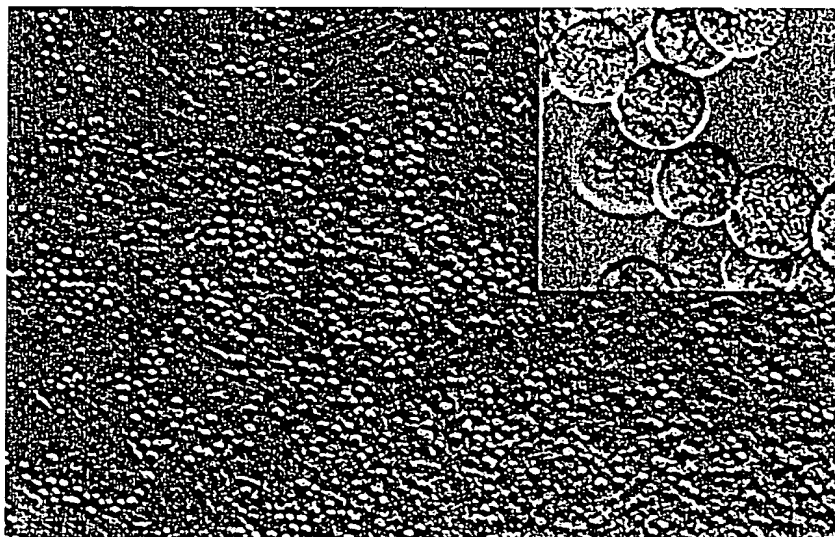


Fig. 4B



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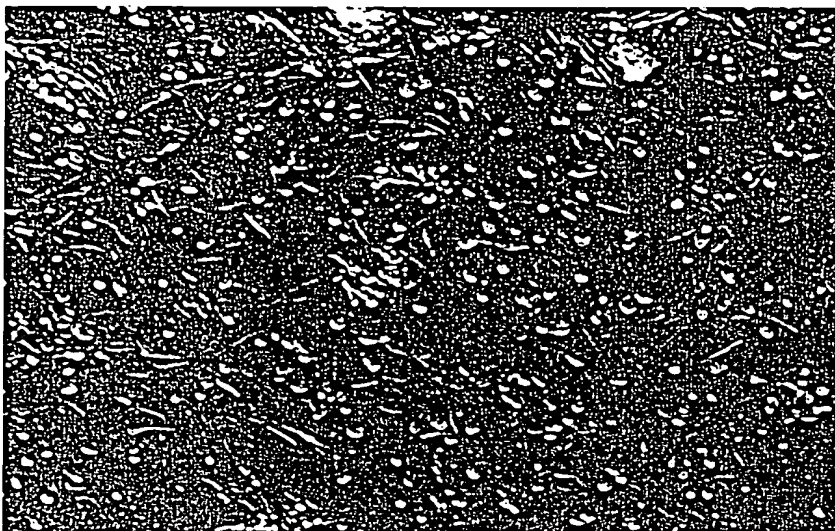


Fig. 4C

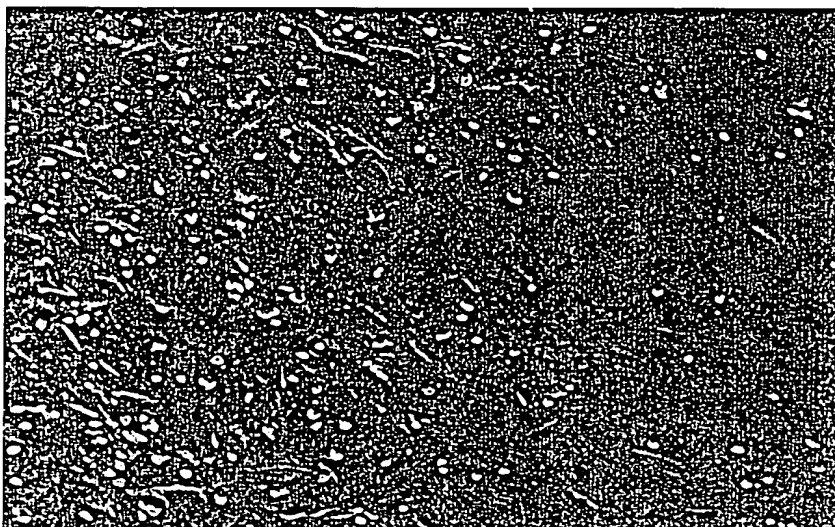


Fig. 4D



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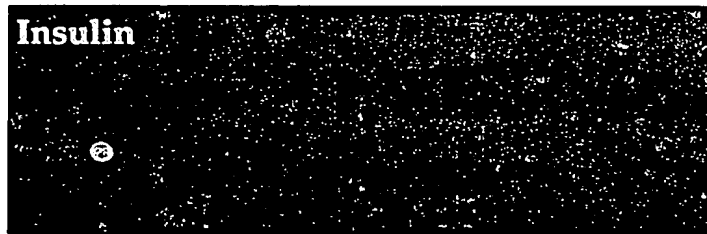


Fig. 5A



Fig. 5B

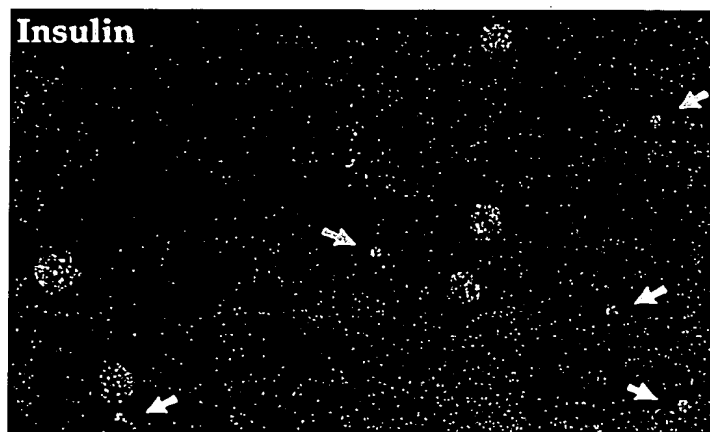


Fig. 5C





Fig. 5D



Fig. 5E

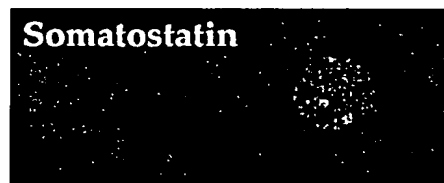


Fig. 5F

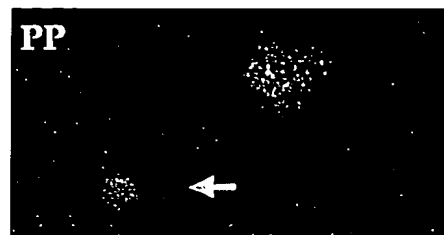


Fig. 5G

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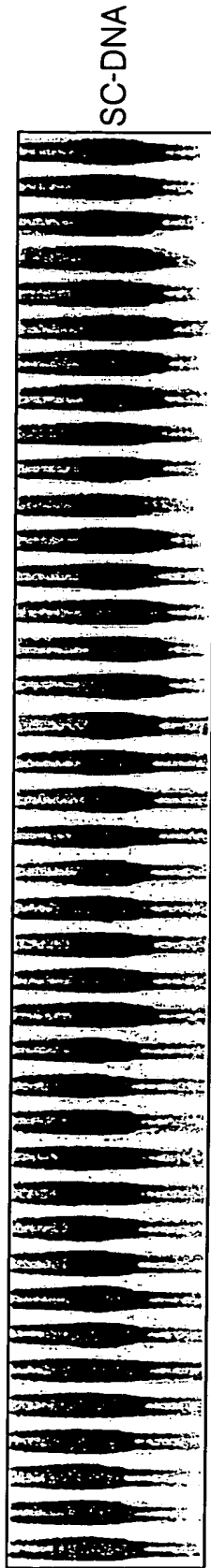


Fig. 6A

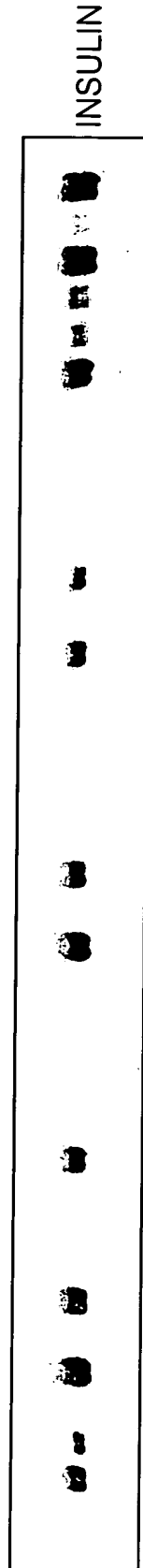


Fig. 6B

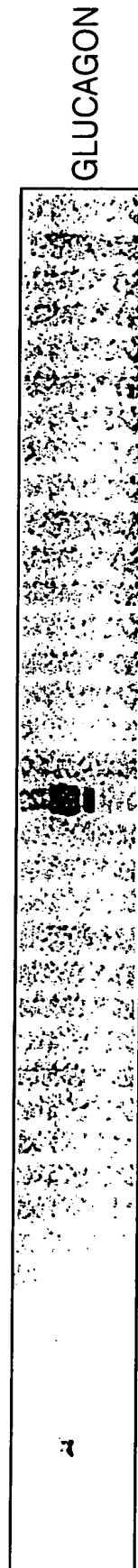


Fig. 6C

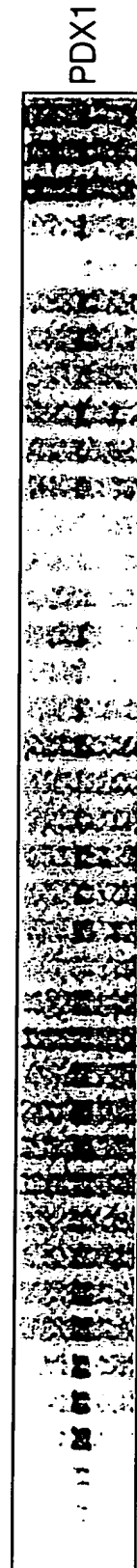


Fig. 6D



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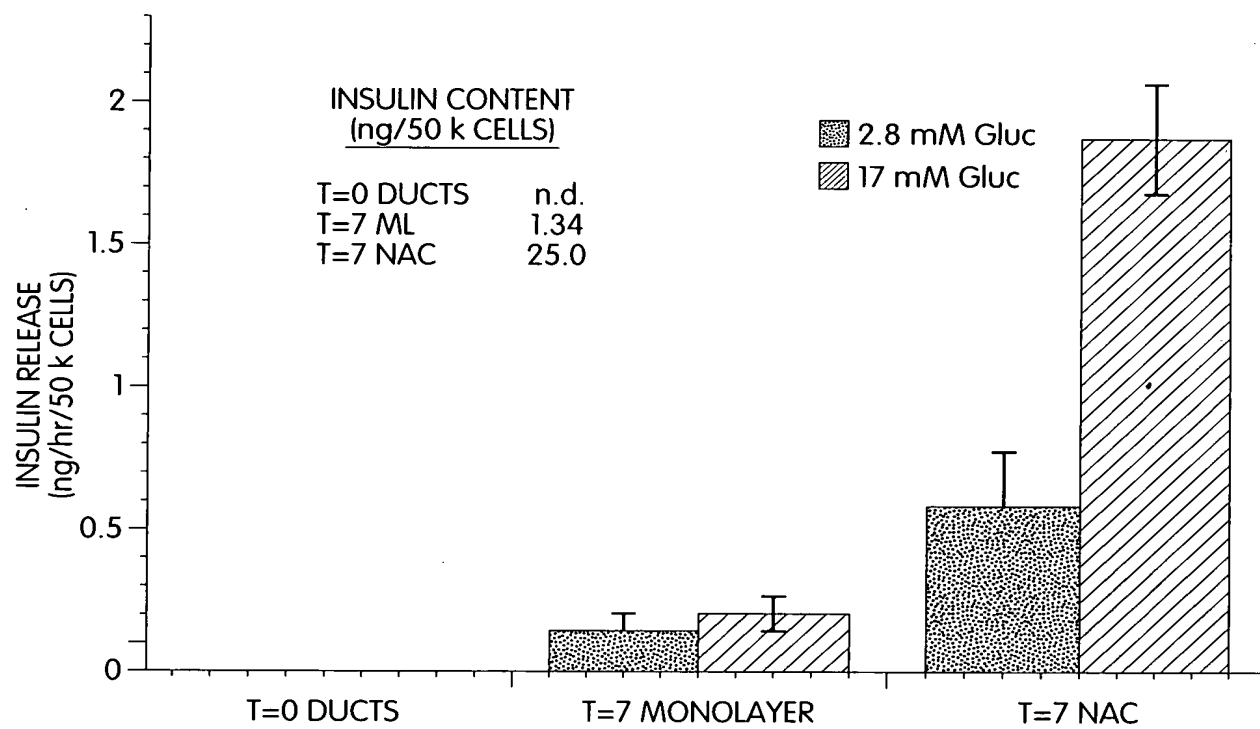


Fig. 7



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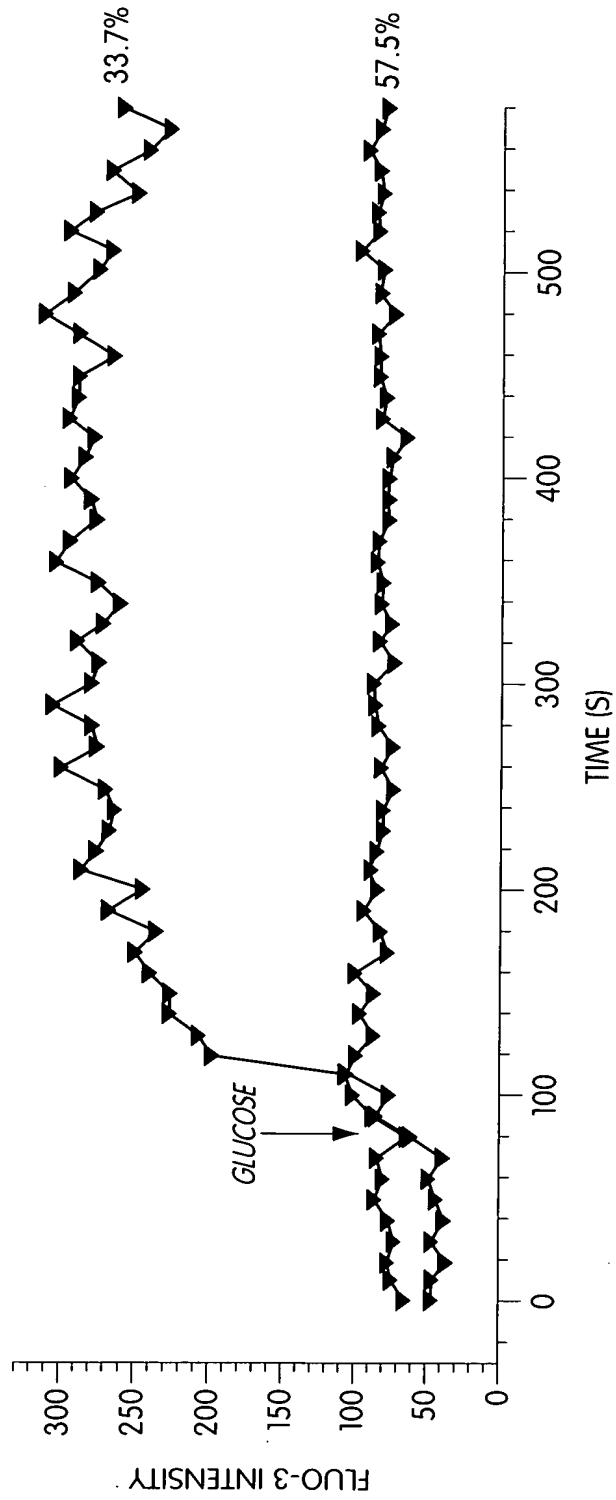


Fig. 8A



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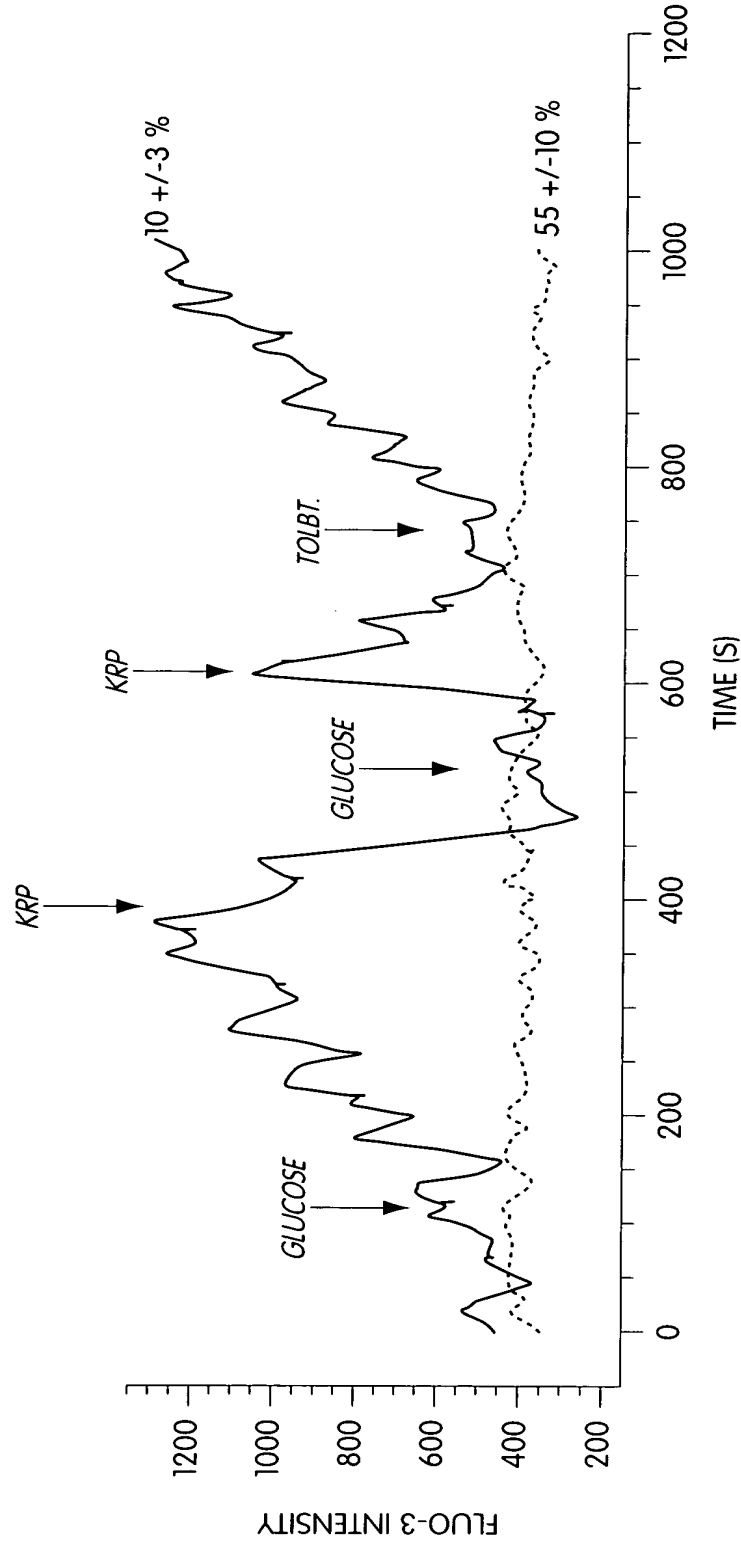


Fig. 8B



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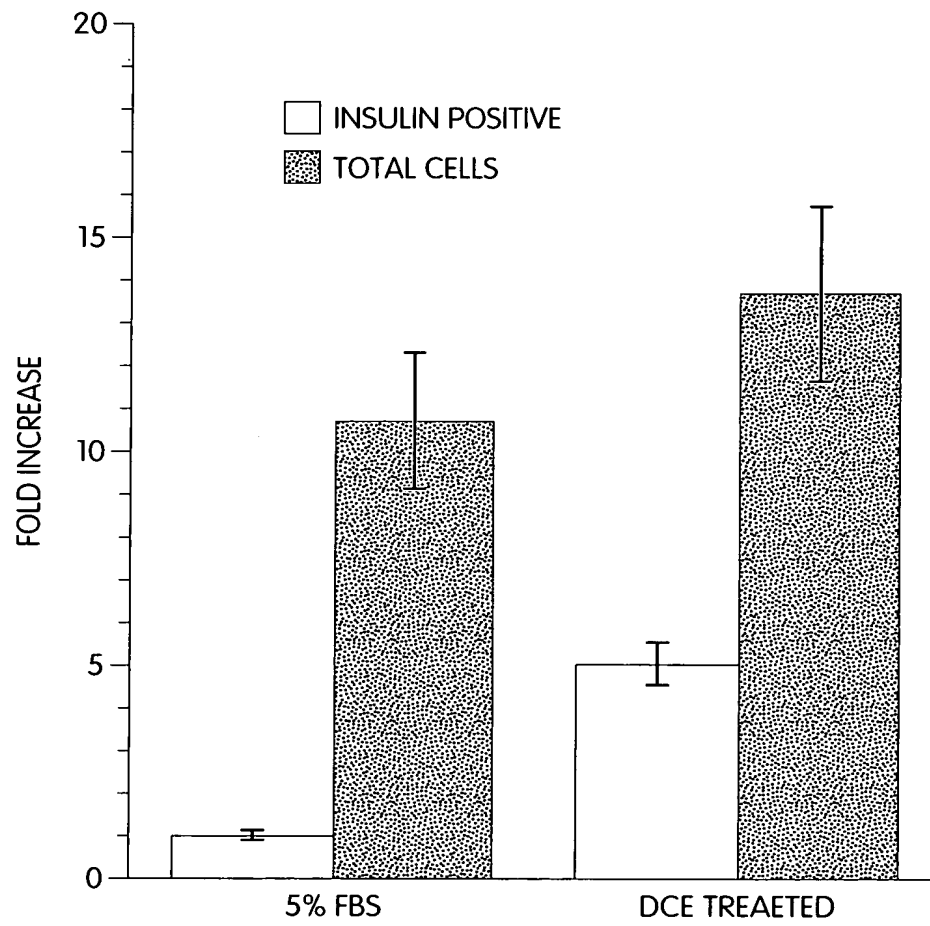


Fig. 9



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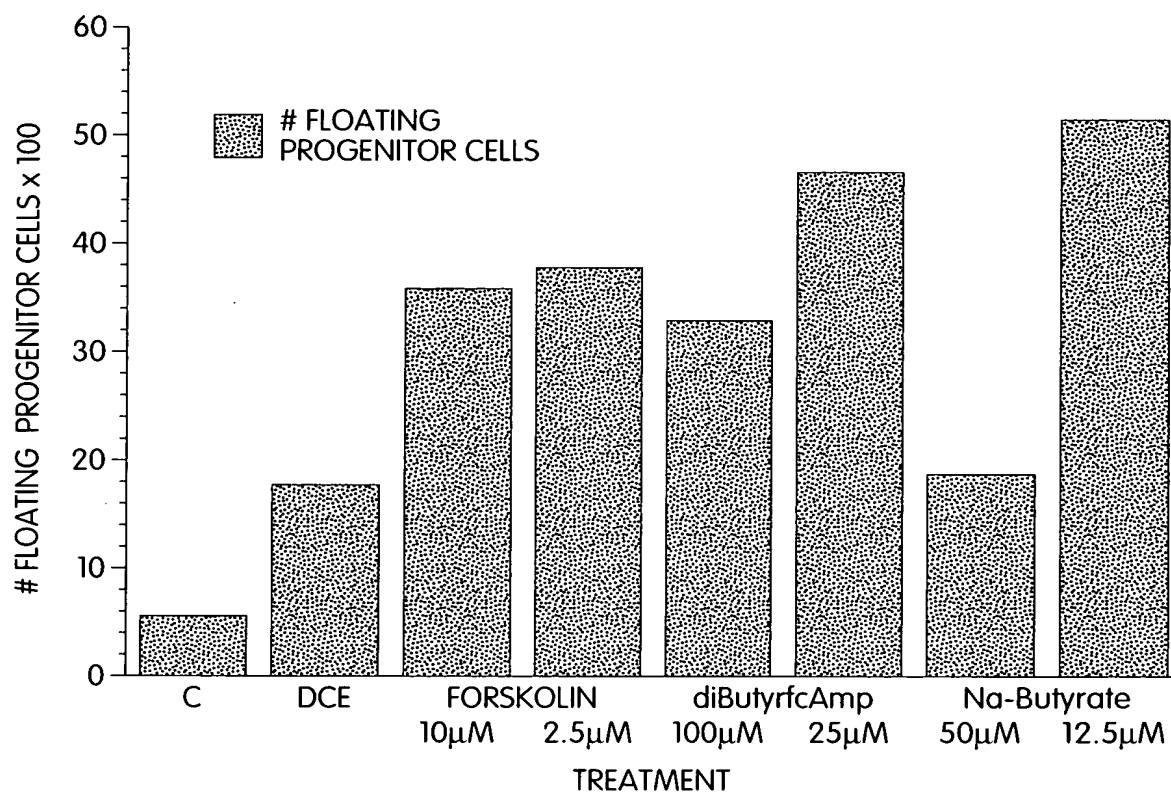


Fig. 10



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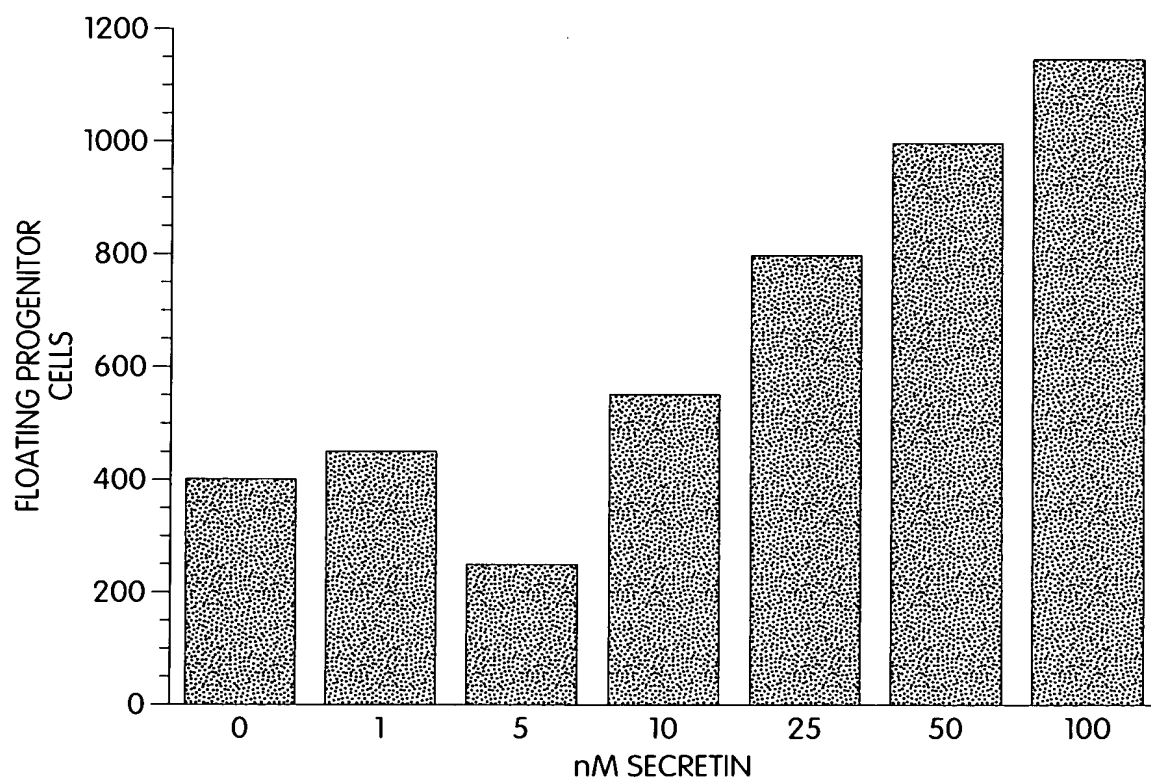


Fig. 11





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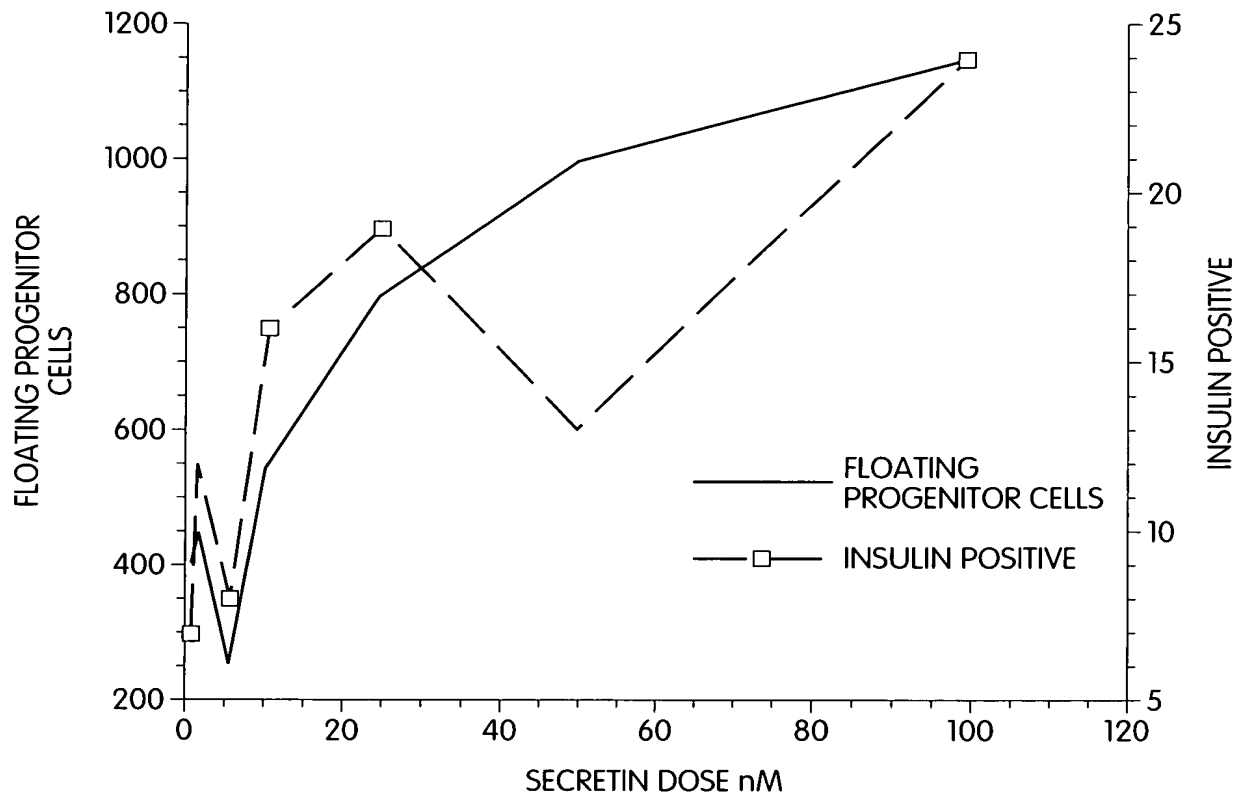


Fig. 12



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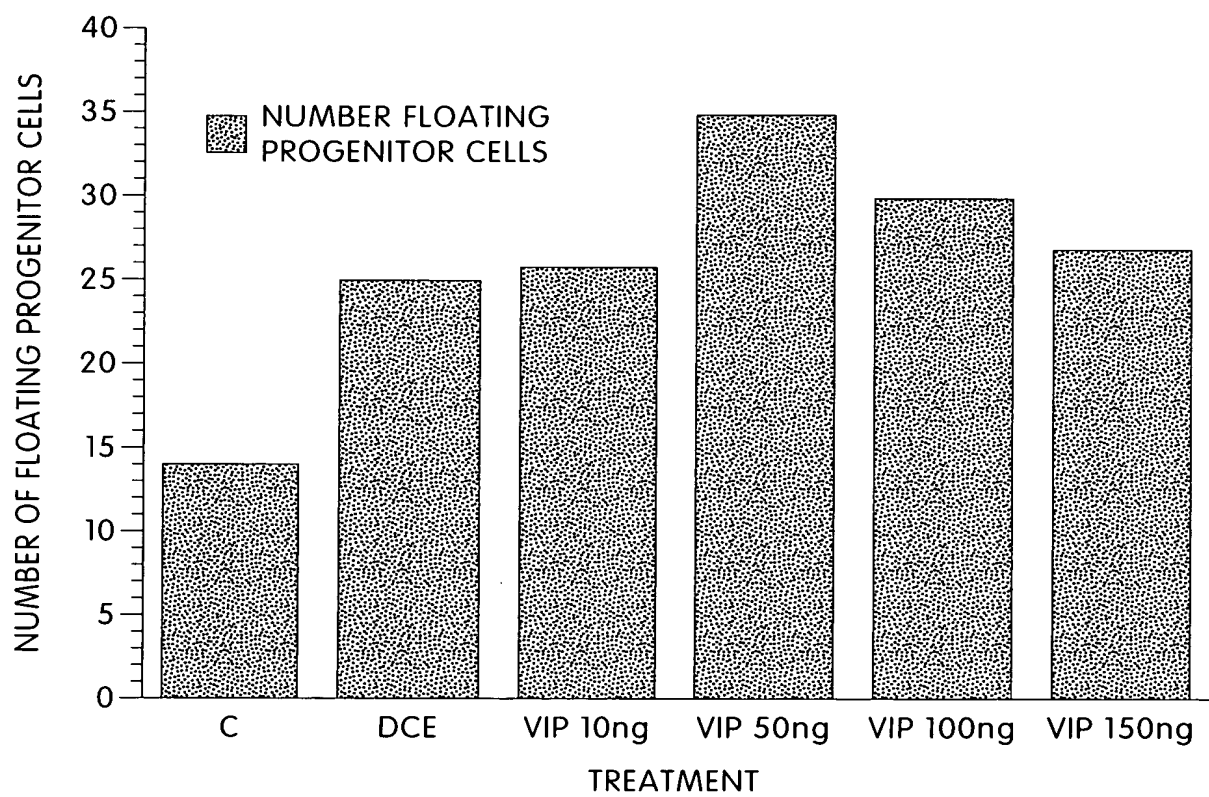


Fig. 13



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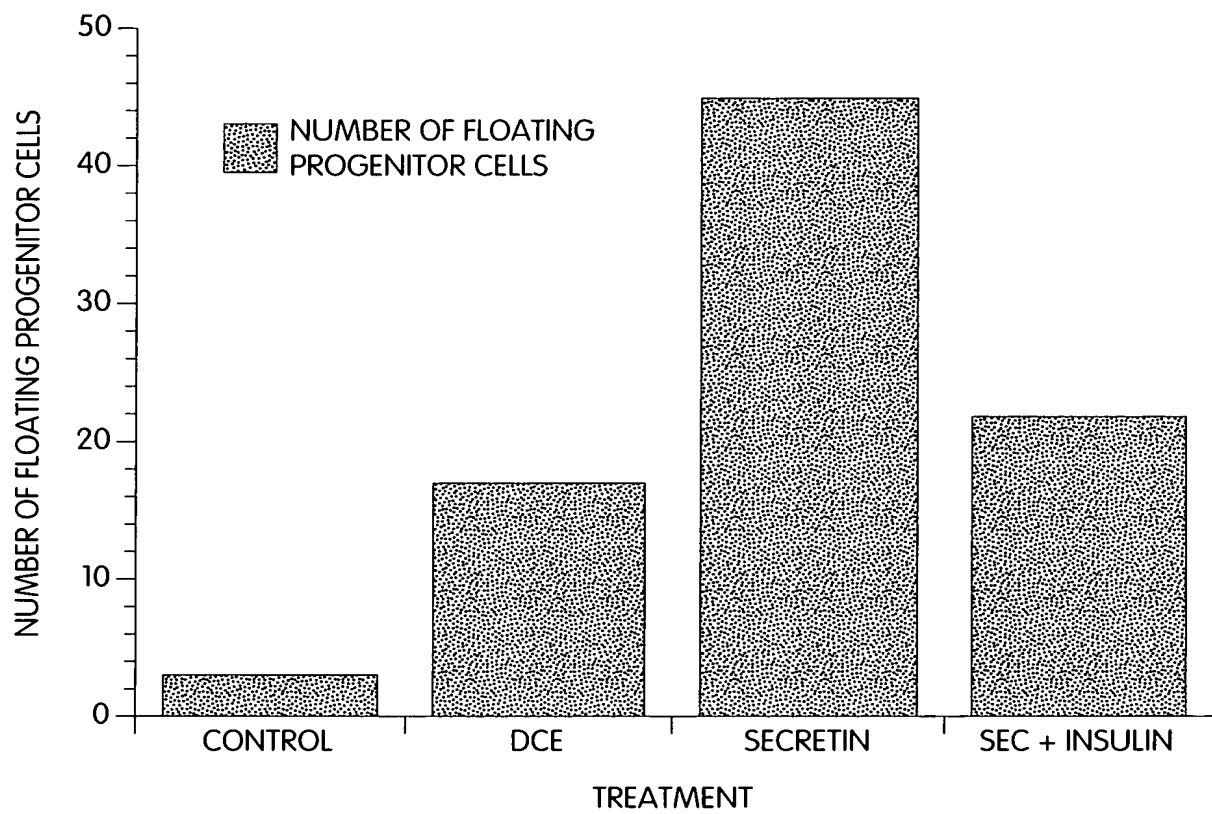


Fig. 14

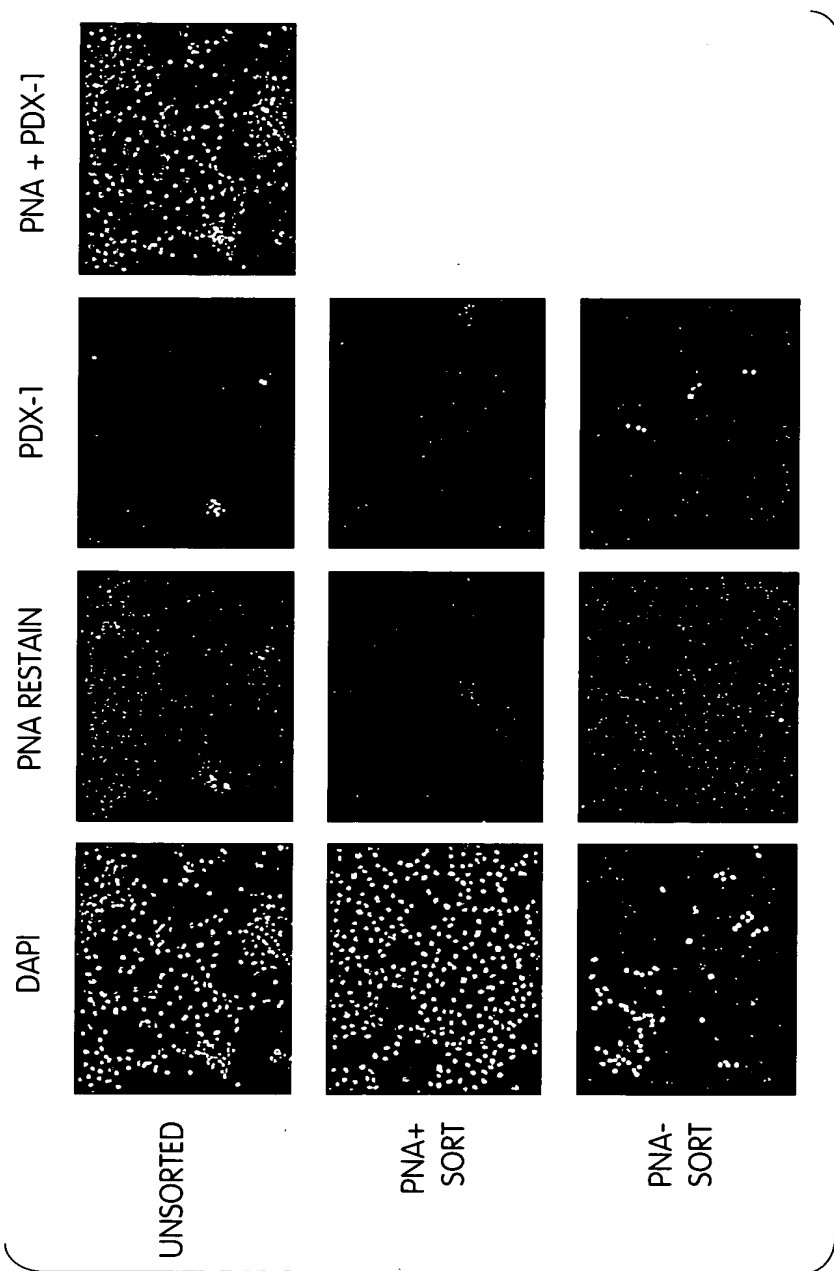
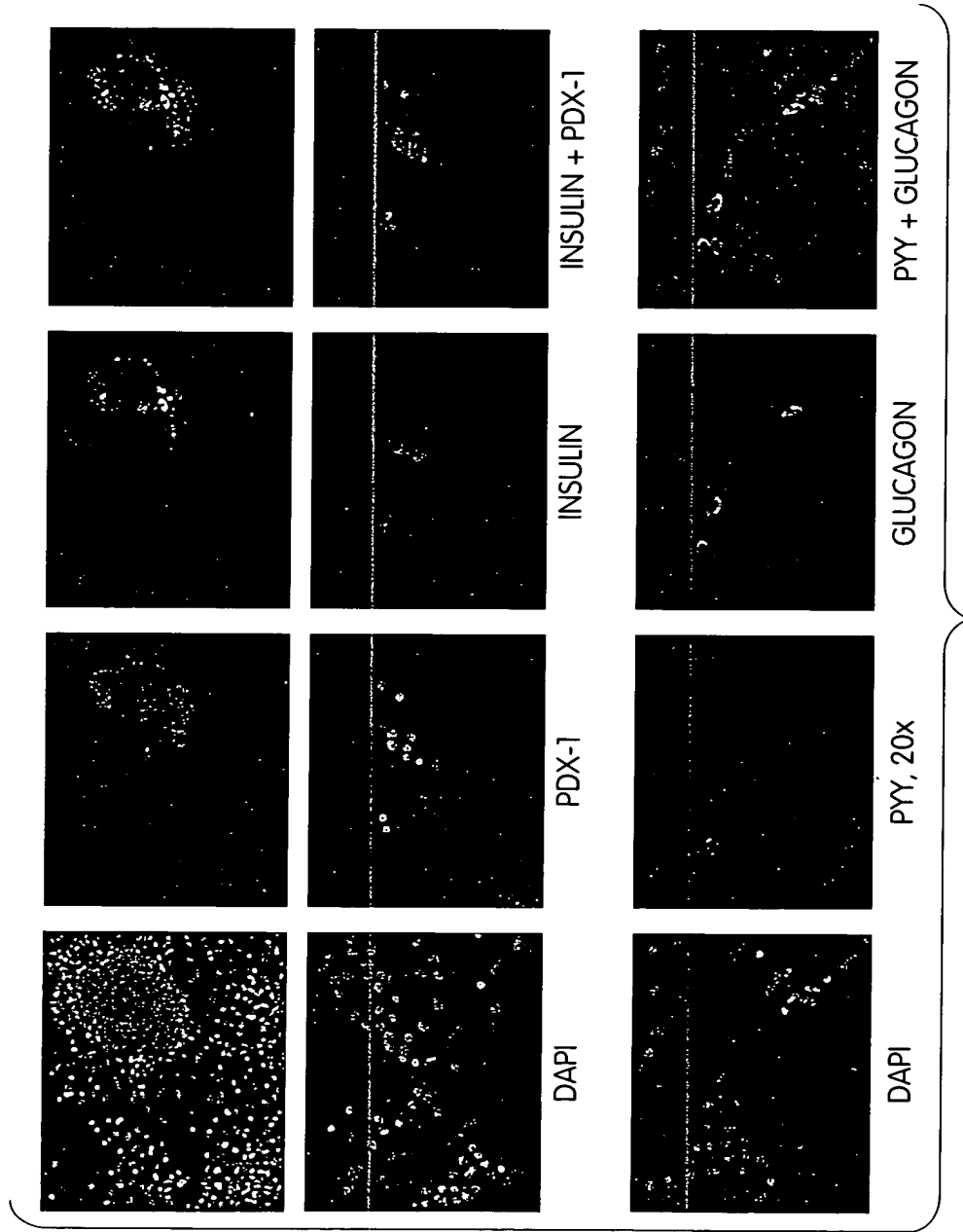


Fig. 15



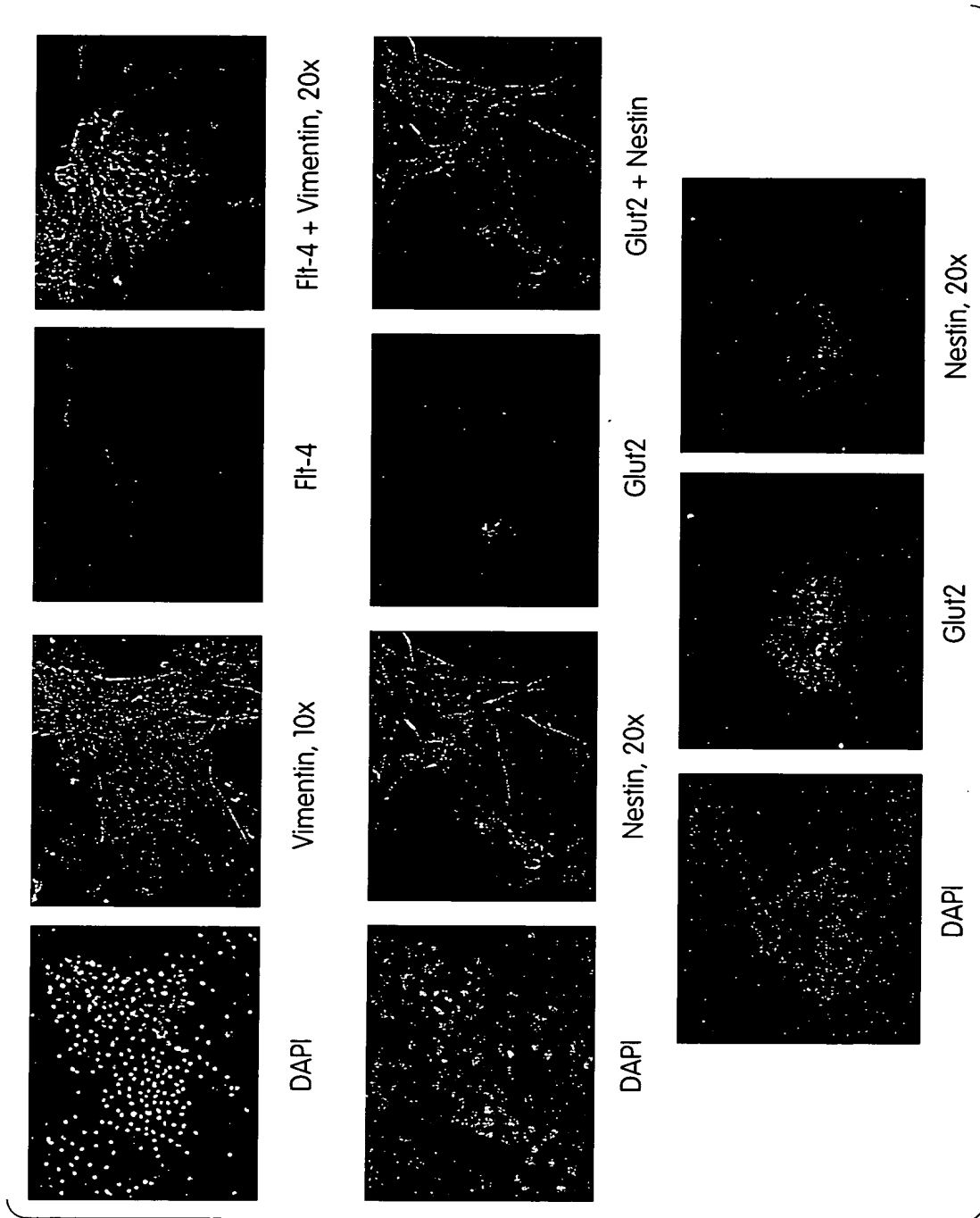


Fig. 17

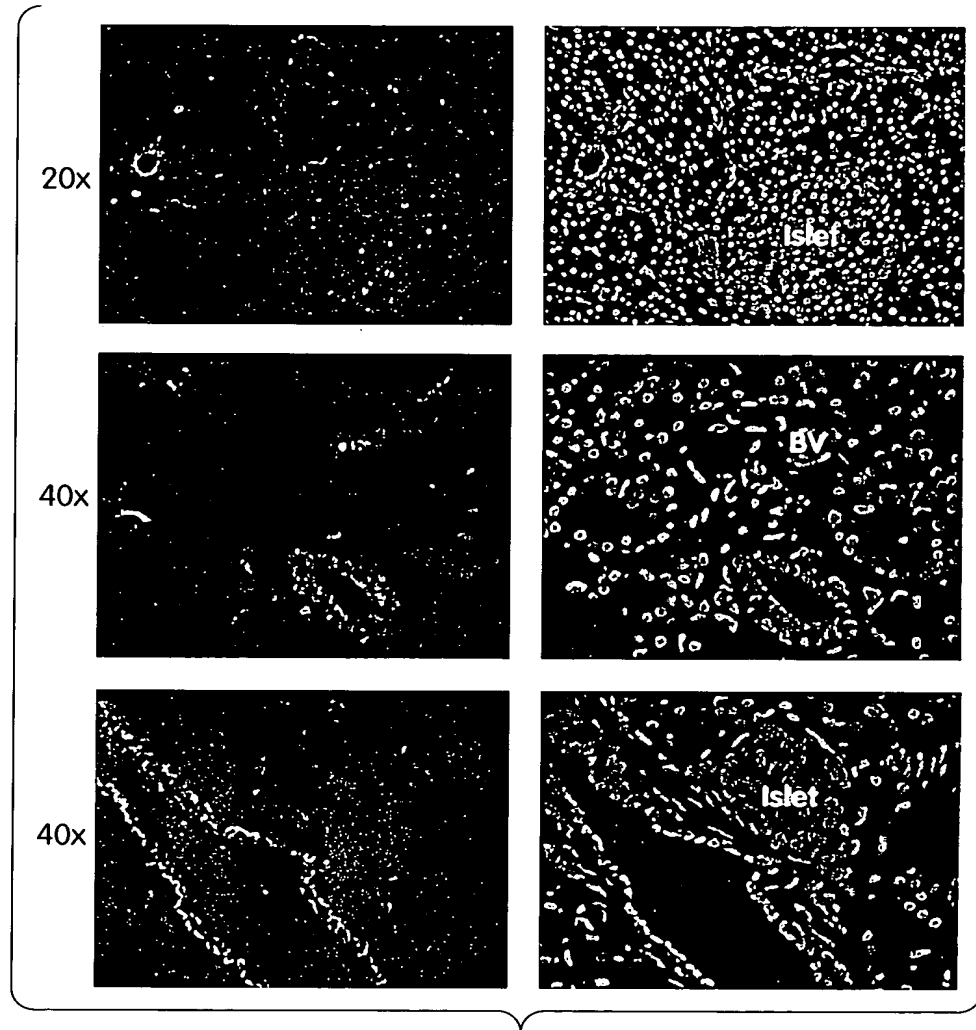


Fig. 18

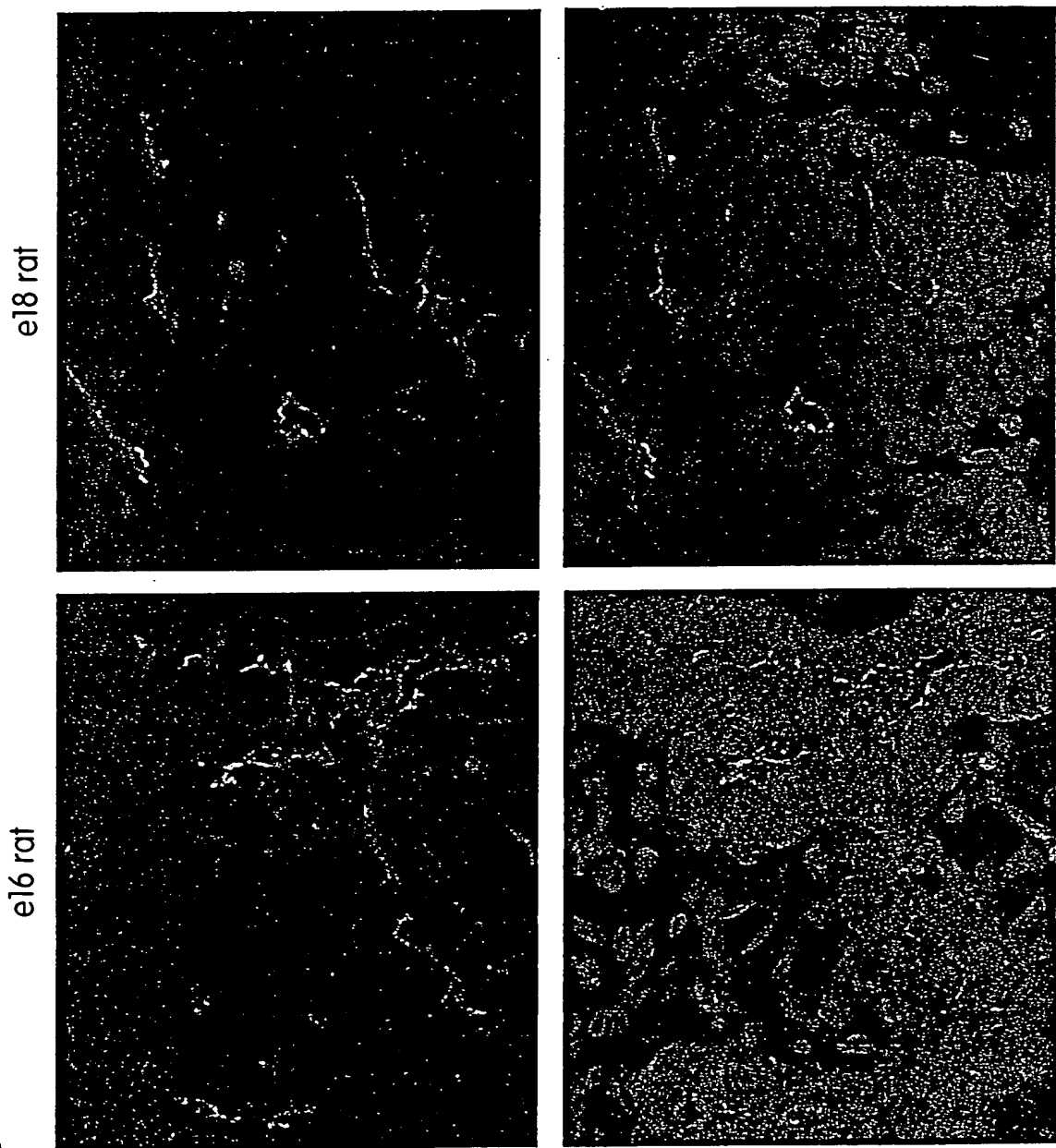


Fig. 19



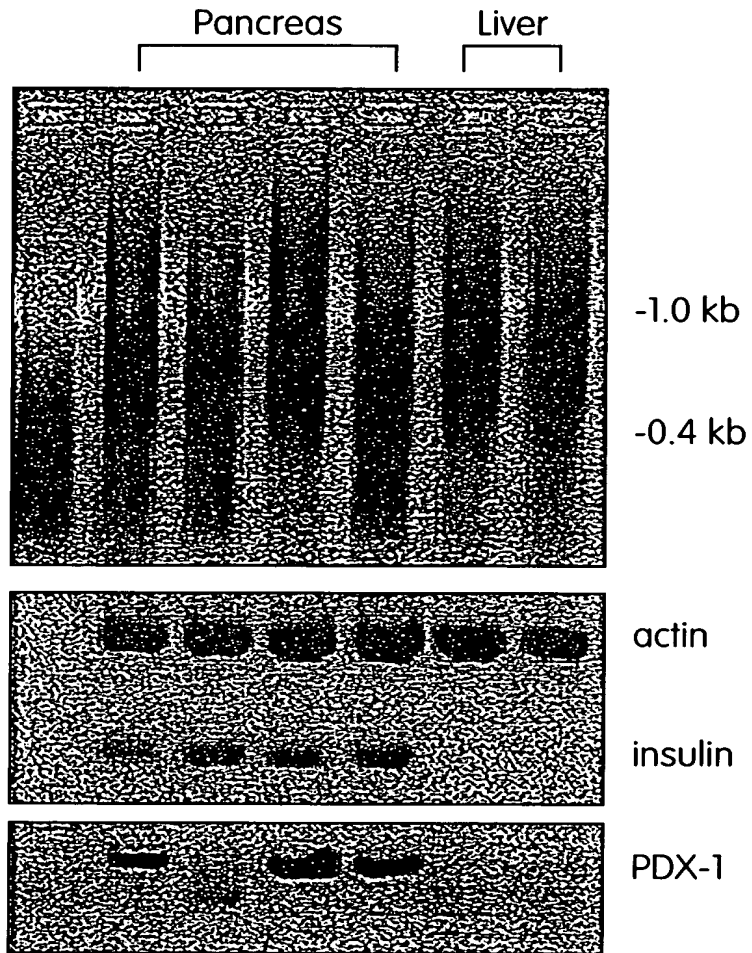


Fig. 20



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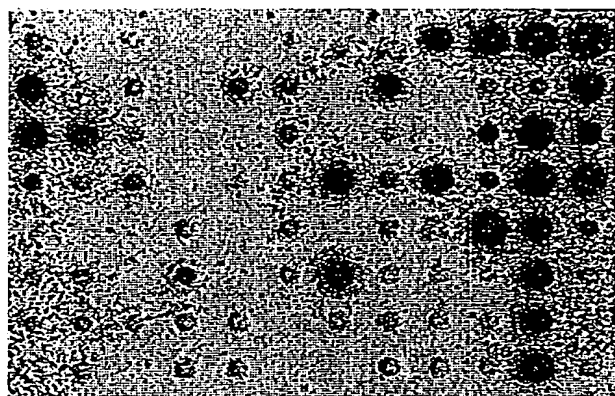
	E13			E14			E15			E16		
	#6	#7	#11	#4	#8	#14	#7	#8	#14	#23	#24	#30
INSULIN	-	-	+	+	+	-	+	+	-	+	+	-
PDX-1	+	+	-	+	-	-	+	-	-	-	-	-
GLUCAGON	±	±	+	+	±	-	-	-	-	-	-	-
AMYLASE	+	±	±	+	+	±	+	+	+	±	+	+
ACTIN	+	+	+	+	+	+	+	+	+	+	+	+
CYCLOPHILIN	+	+	+	+	+	+	+	+	+	+	+	-

Fig. 21

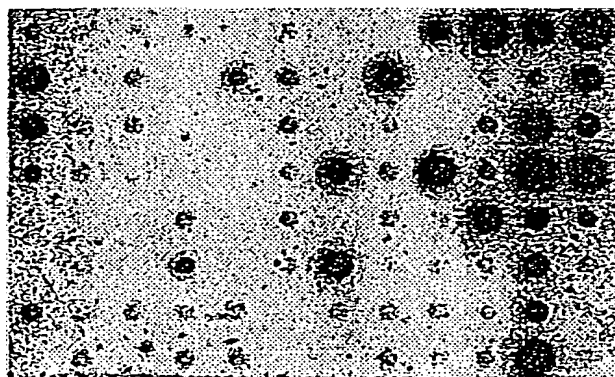


	1	2	3	4	5	6	7	8	9	10	11	12
A	actin	HexoK	PYY	TyrH	SHH	Wnt3	delta	IGF1	TNFR2	PICK1	amphy2	Rho-GDI
B	G3PDH	SubPR	NPY	Rab3A	Patch-1	Wnt5	Jagged	PKA	Pw1	PCTA-RE1	OSF-1	Sez-12
C	G6PDH	insulin	NPYR	activin	SMO	frizzled	DLK	Isl-1	HNF1 $\alpha$	Gli	GP106	SelenoP
D	RPs6	glucagon	Secretin	follistatin	TGF $\beta$ 1	sFRP-1	notch-1	beta2	DCoH	P48	HCNGP	Surf-1
E	Glut4	SomS	nestin	activinR	TGF $\beta$ 2	EGF	notch-2	PDX1	HNF3 $\beta$	ID-1	clusterin	VASP
F	albumin	PP	Chromo graninA	BMB4	TGF $\beta$ RI	EGFR	FGF6	Pax4	HNF4 $\alpha$	IDR	Cab45b	UK-2
G	amylase	IAPP	GLP-IR	BMB4R	PTHrP	SCF	FGF9	Pax6	Nkx2.2	MITF	HBP	UK-4
H	CarbP	Glut2	CK19	BMB6	PTHR	c-Kit	FGFR1	COUP-TFII	Nkx6.1	SUG1	RP2	UK-6

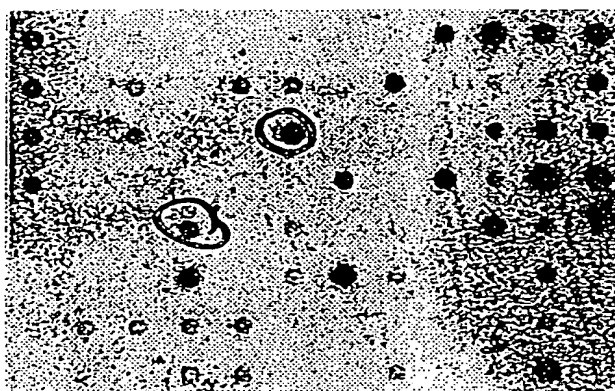
Fig. 22



islet



E15 ins+/PDX+



heart

Fig. 23



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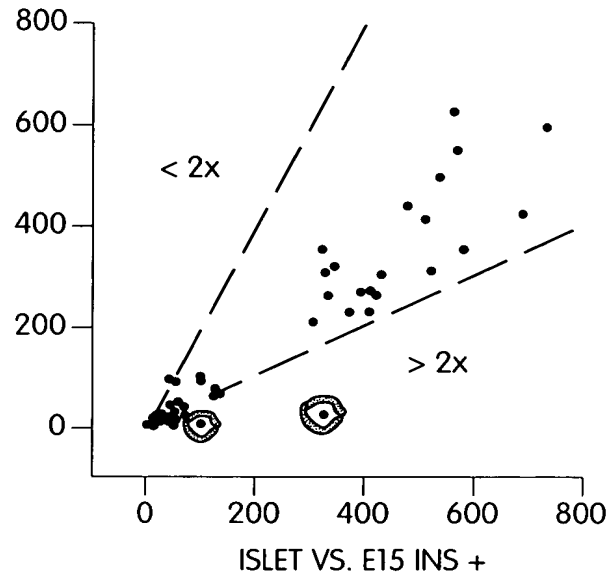


Fig. 24A

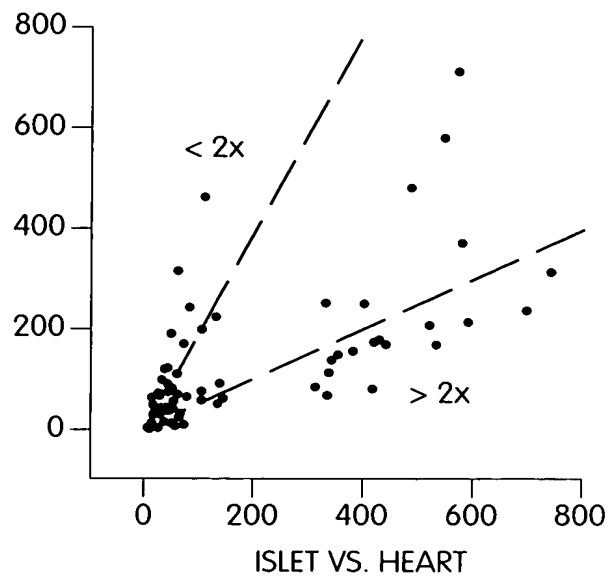


Fig. 24B



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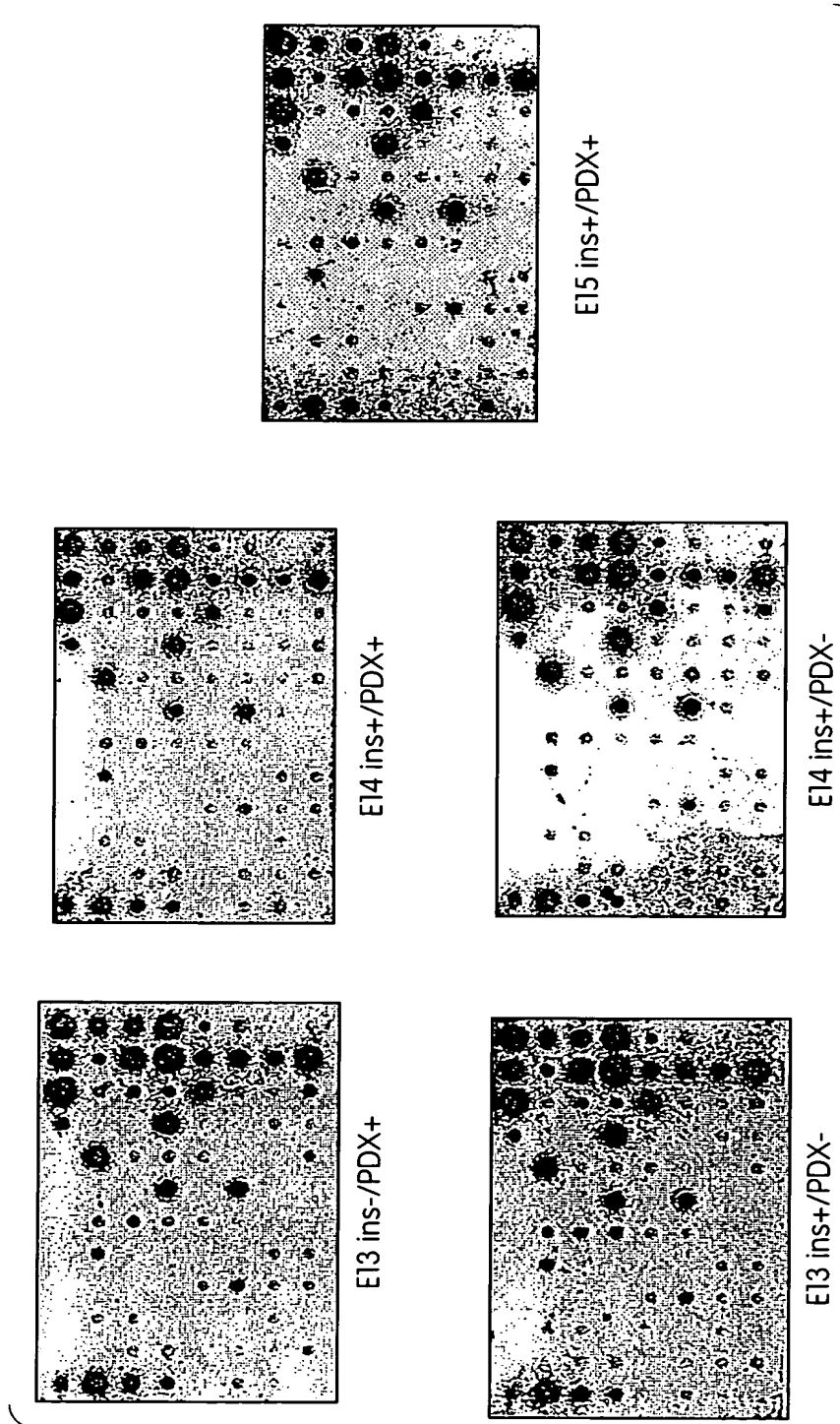


Fig. 25



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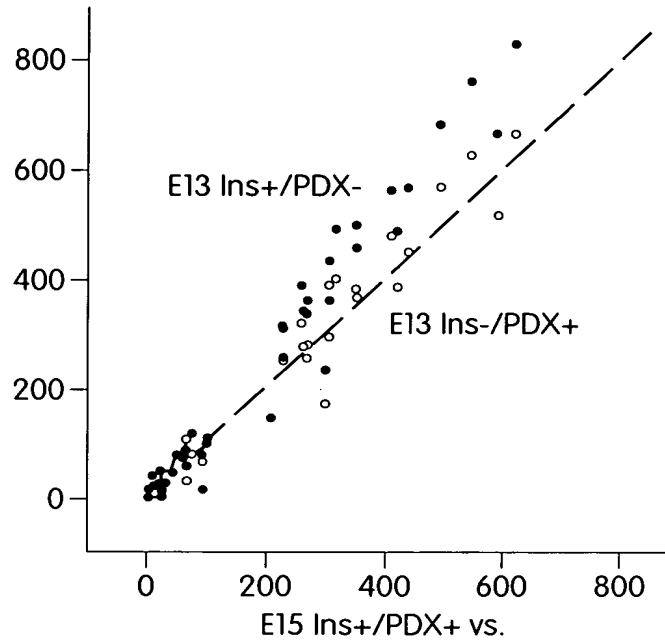


Fig. 26A

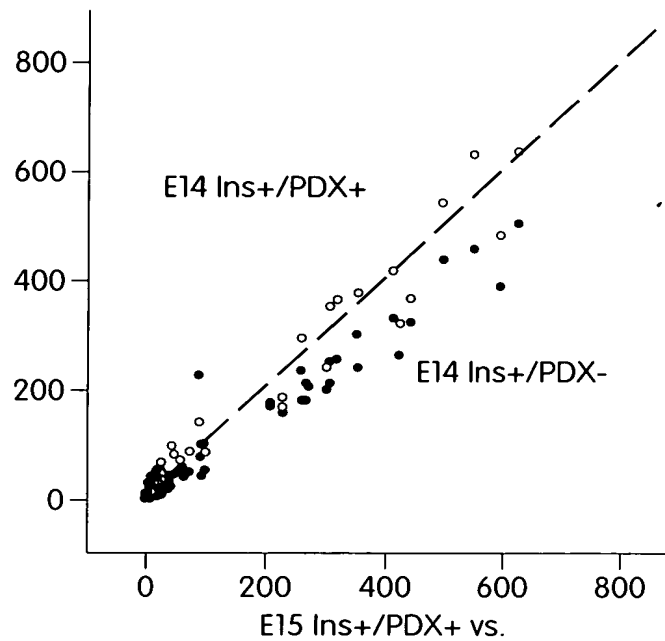
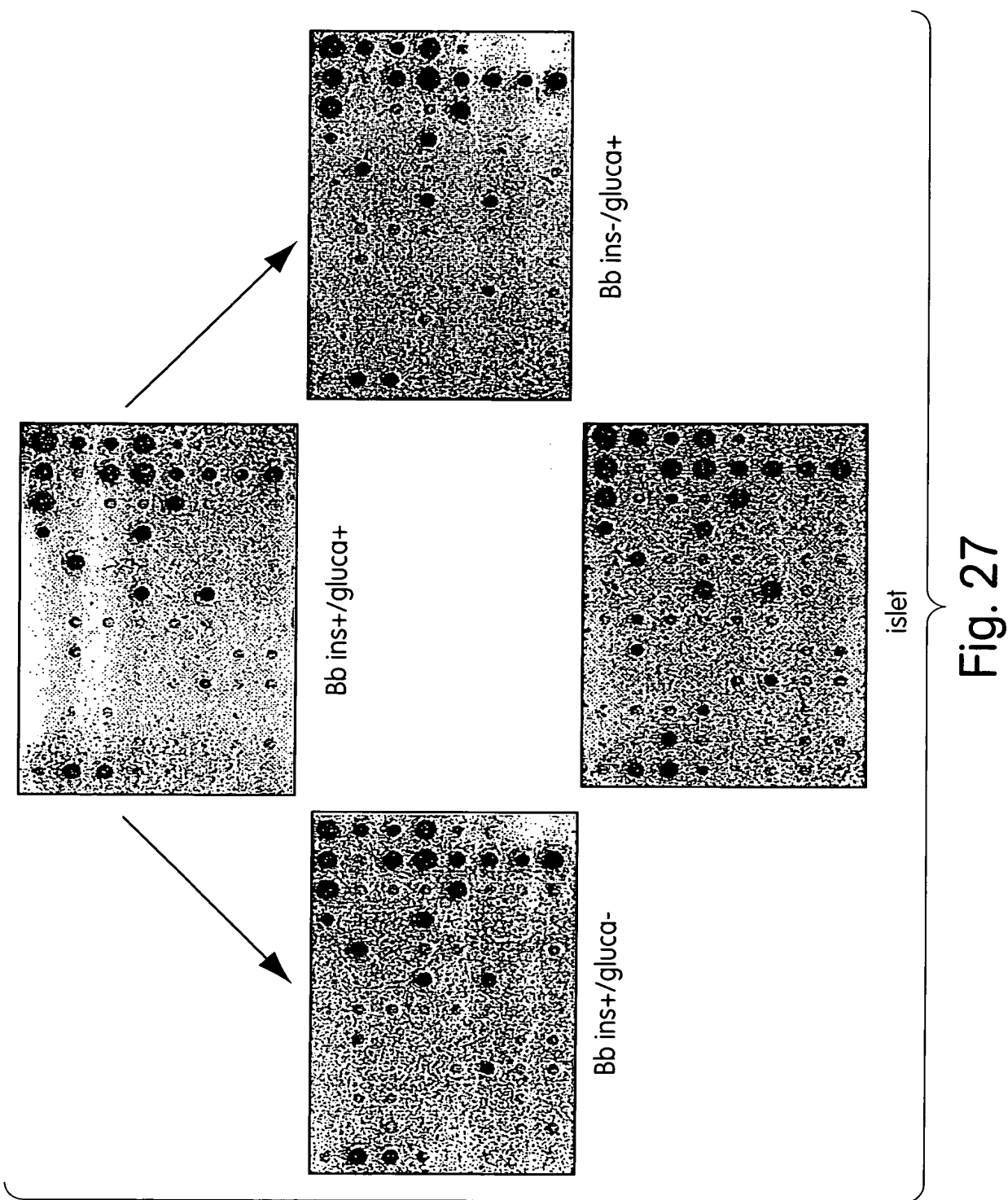


Fig. 26B







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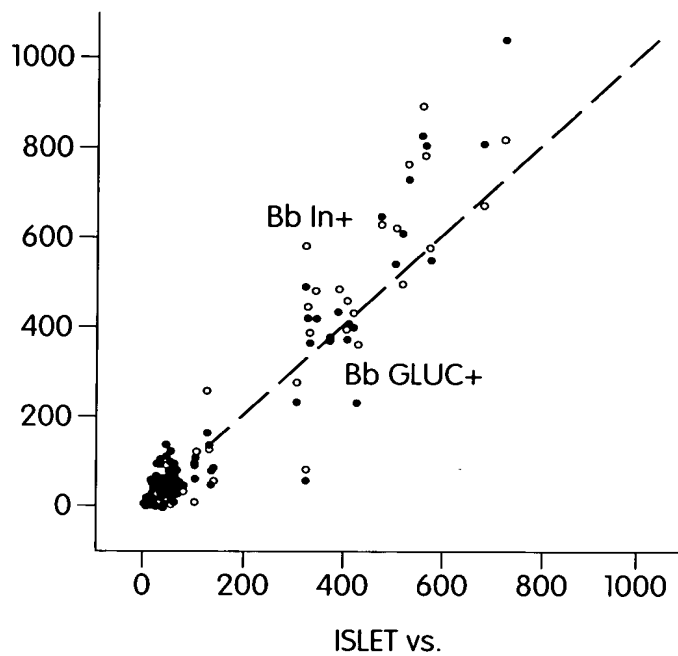


Fig. 28A

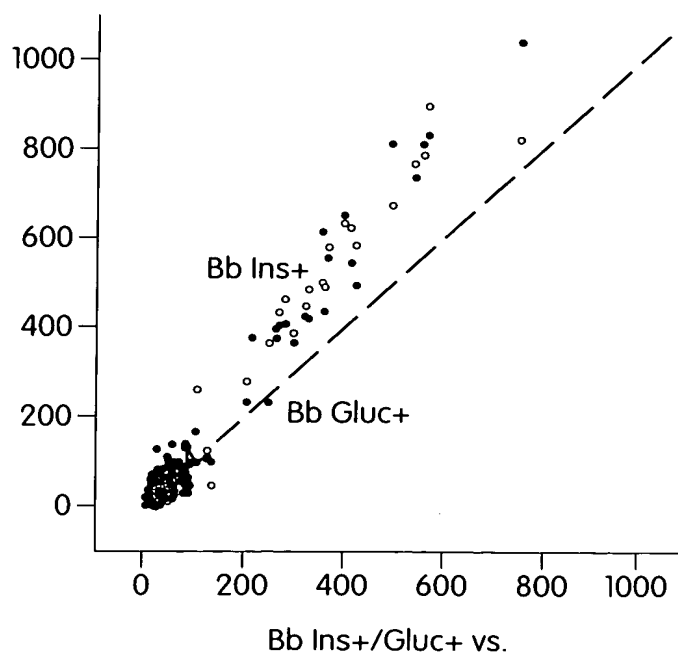


Fig. 28B



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<u>GENE NAME</u>	<u>ISLET/E15 Ins+</u>	<u>ISLET/Bb Ins+</u>
Secretin	16	8
insulin	13	4
glucagon	3	2
IGF1	6	6
nestin	5	3
Rab3A	5	2
Glut2	2	1.3
ChromograninA	4	3
PDX1	3	2
Isl-1	2	2
EGF	4	2
NPYR	4	1.3
TGFb1	4	3
TGFbR1	6	2
delta	26	18
DLK	3	4
Wnt3	3	2
Gli	2	2
SMO	4	6
COUP-TFII	0.9	1.1

Fig. 29



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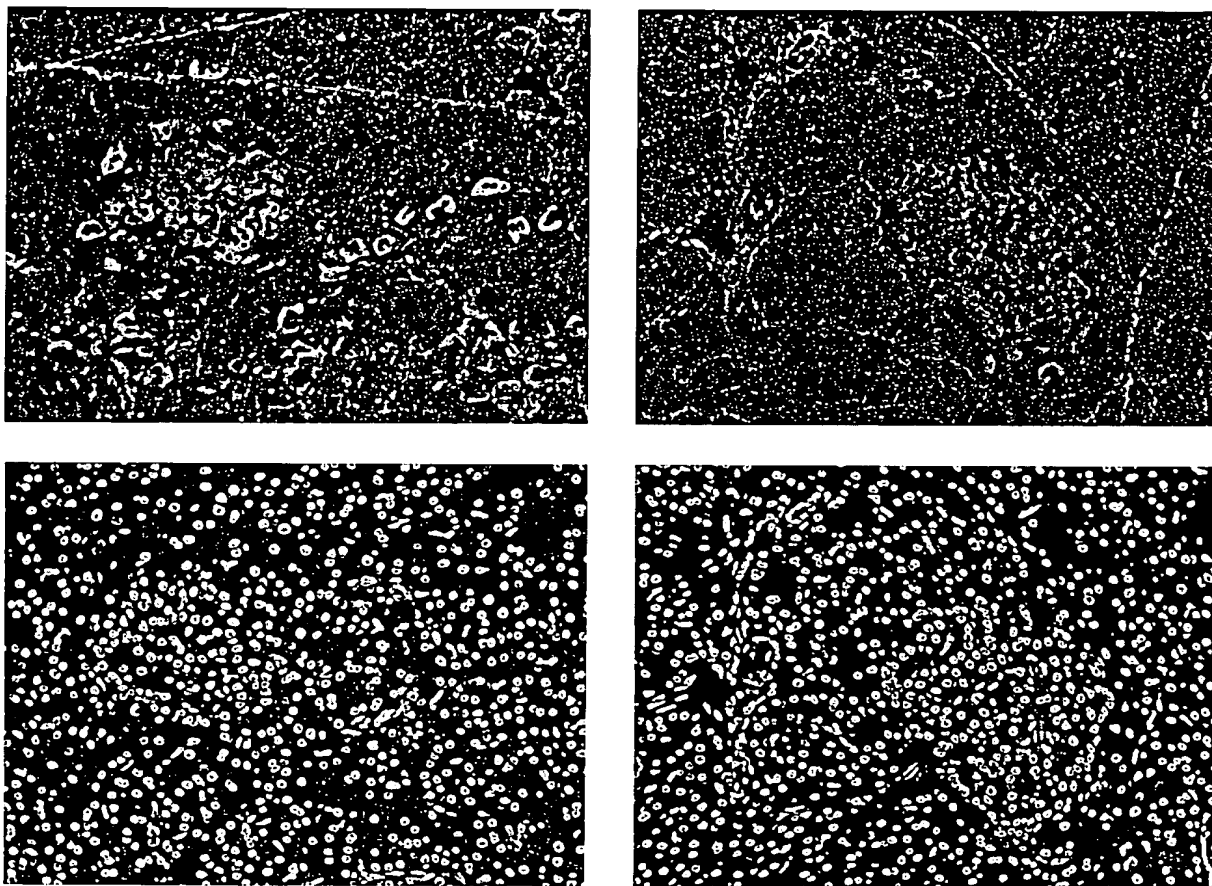


Fig. 30

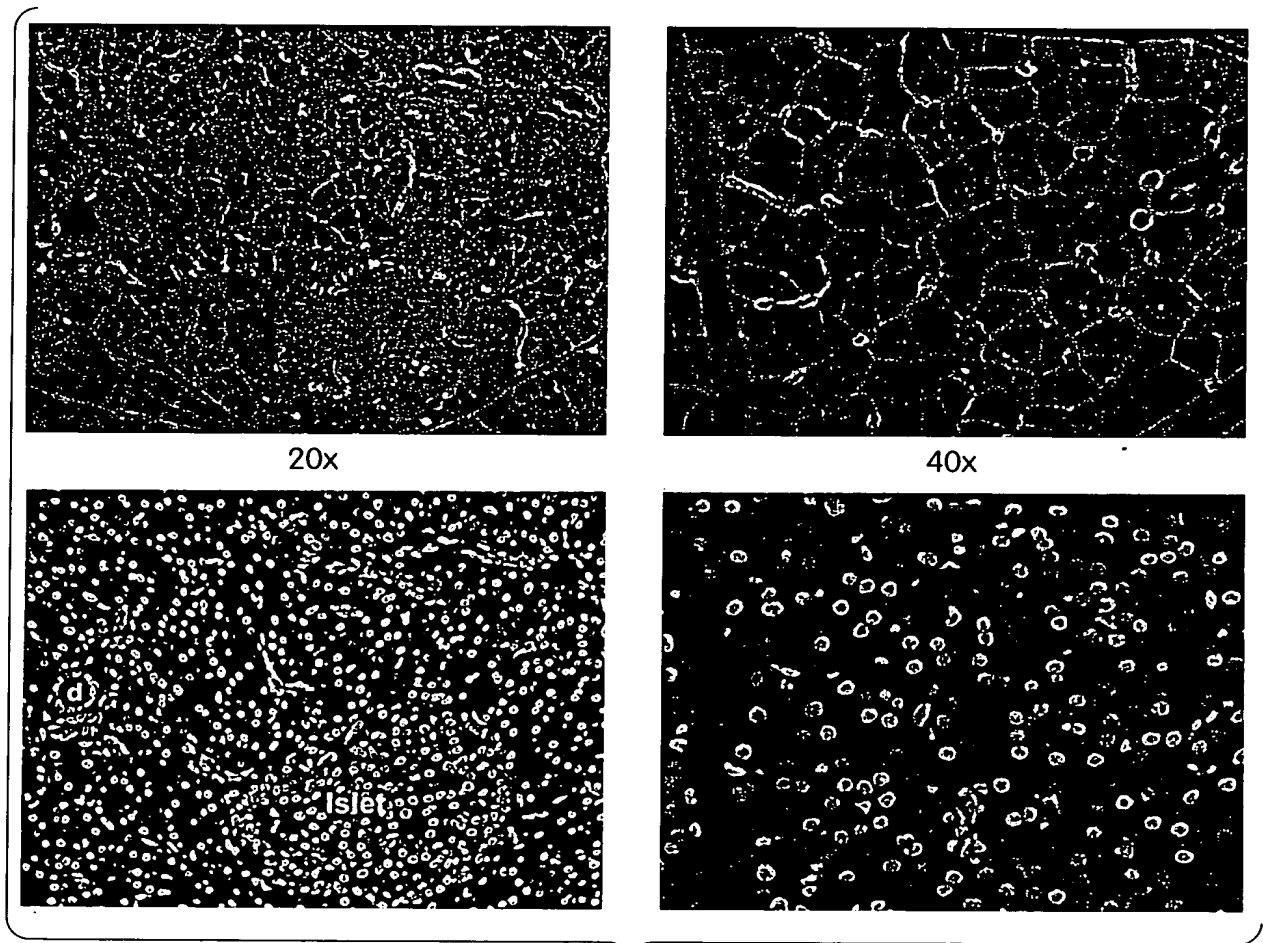


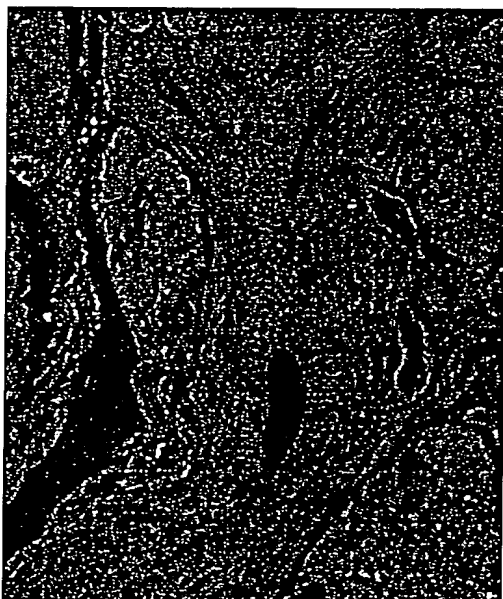
Fig. 31



Subpopulation of Epithelium



Interlobular Duct, 40x



Interlobular Ducts, 20x (Negative)



Positive Epithelial Cells

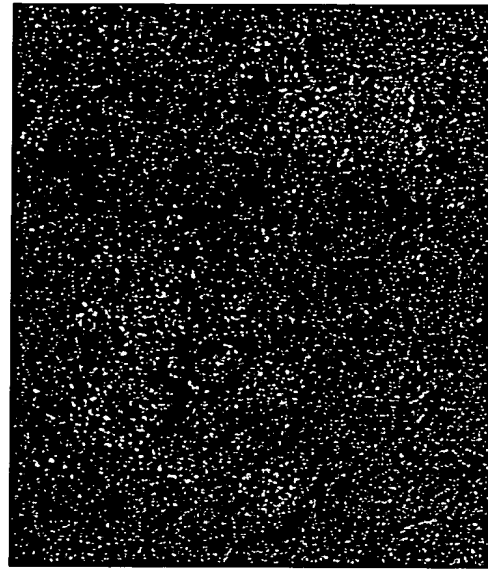
Fig. 32



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Interlobular Duct, 20x



Islets, 20x



Interlobular Duct, 40x

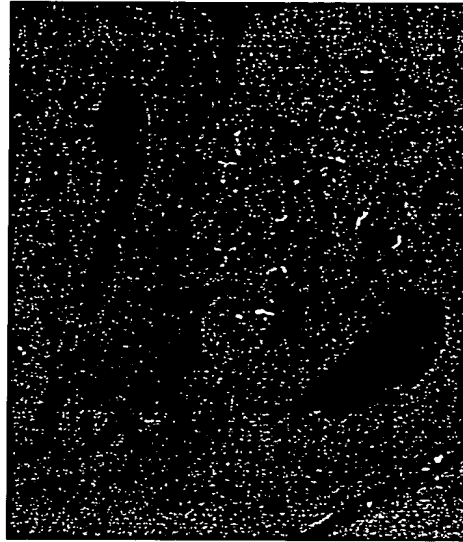


DAPI

Fig. 33



LCA, Lens culinaris Agglutinin



ECL, Erythrina cristagalli Lectin



DSL, Datura stramonium

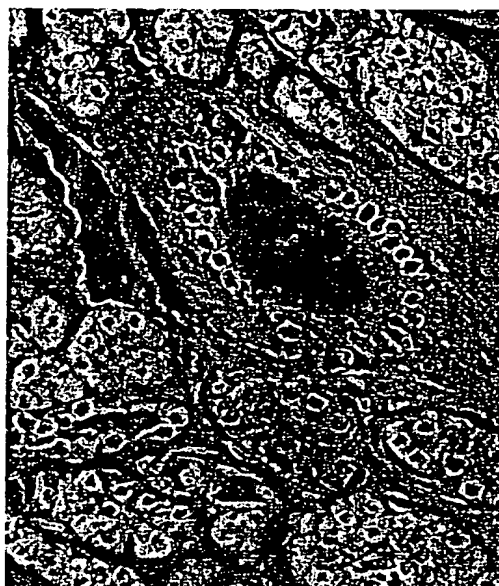


Succinylated-WGA

Fig. 34



40x, Interlobular and Intralobular Ducts



20x, Intralobular Ducts

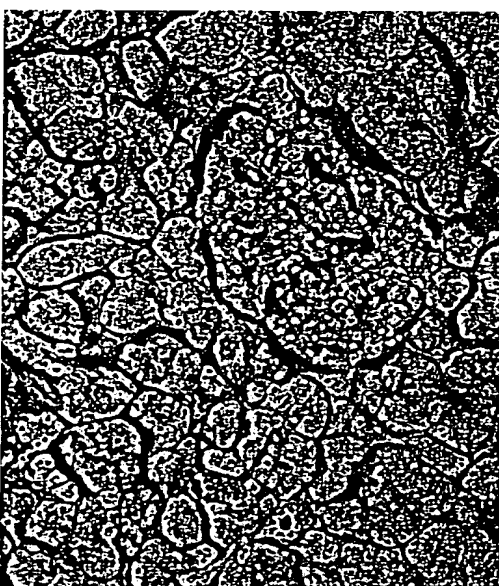
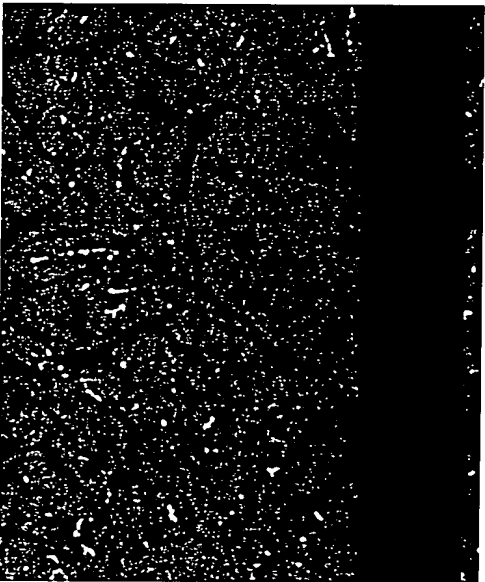


Fig. 35





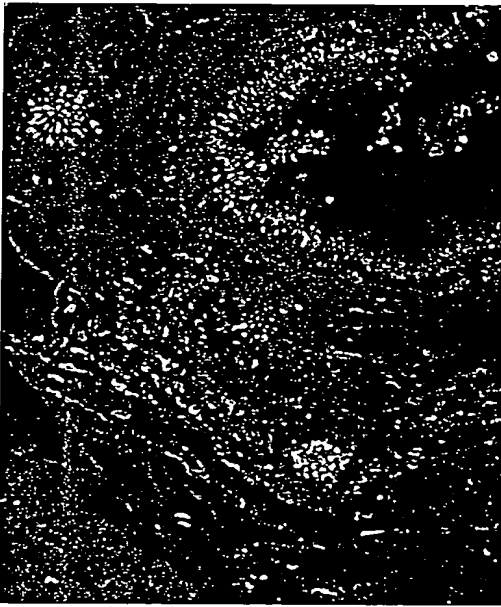
40x, Interlobular and Intralobular Ducts



20x, Interlobular Ducts



Fig. 36



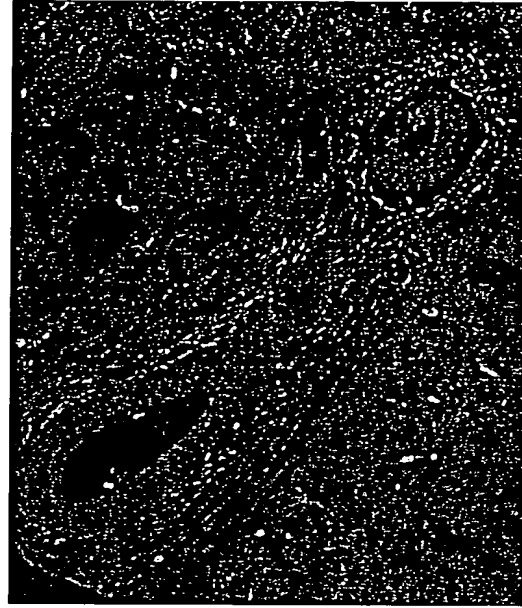
RCA-I, Ducts and Mesenchyme



RCA-II, Small Ductules & Mesenchyme

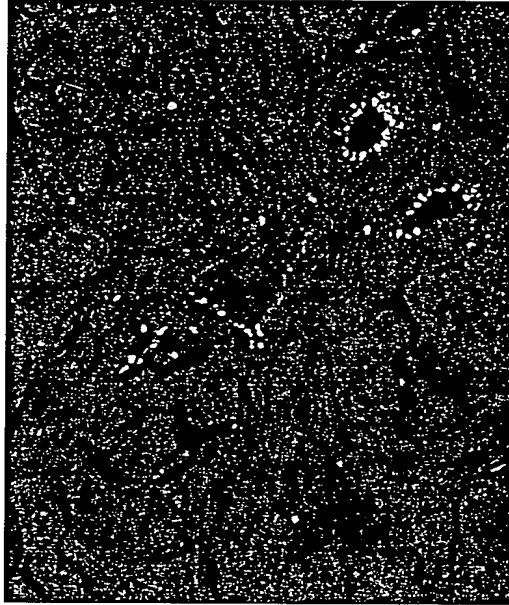


RCA-II, Islets



RCA-II, Small Ductules & Mesenchyme

Fig. 37



Interlobular Ducts, negative Islet, 20x



Main and Interlobular Ducts, 20x



Duct Epithelium, 20x



Main and Interlobular Ducts, 10x

Fig. 38



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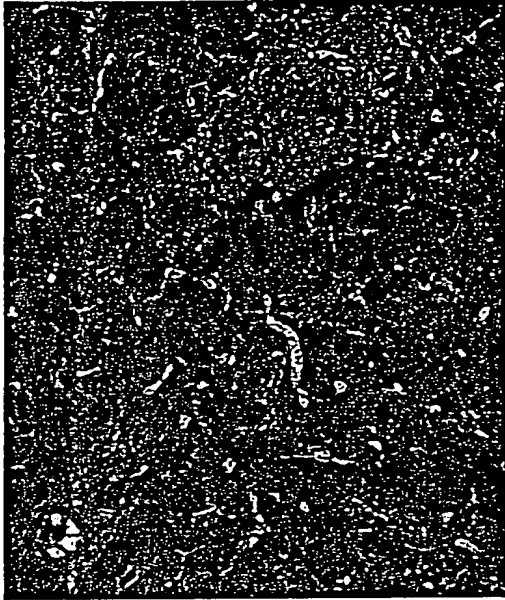


Fig. 39



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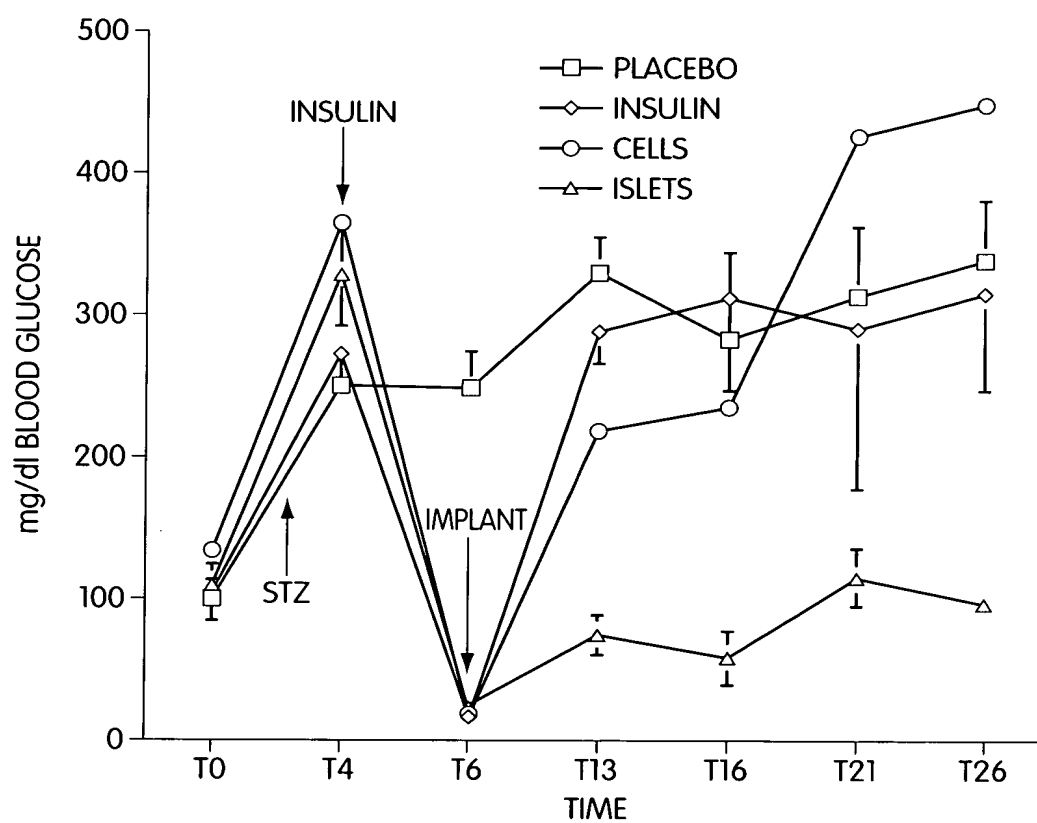


Fig. 40



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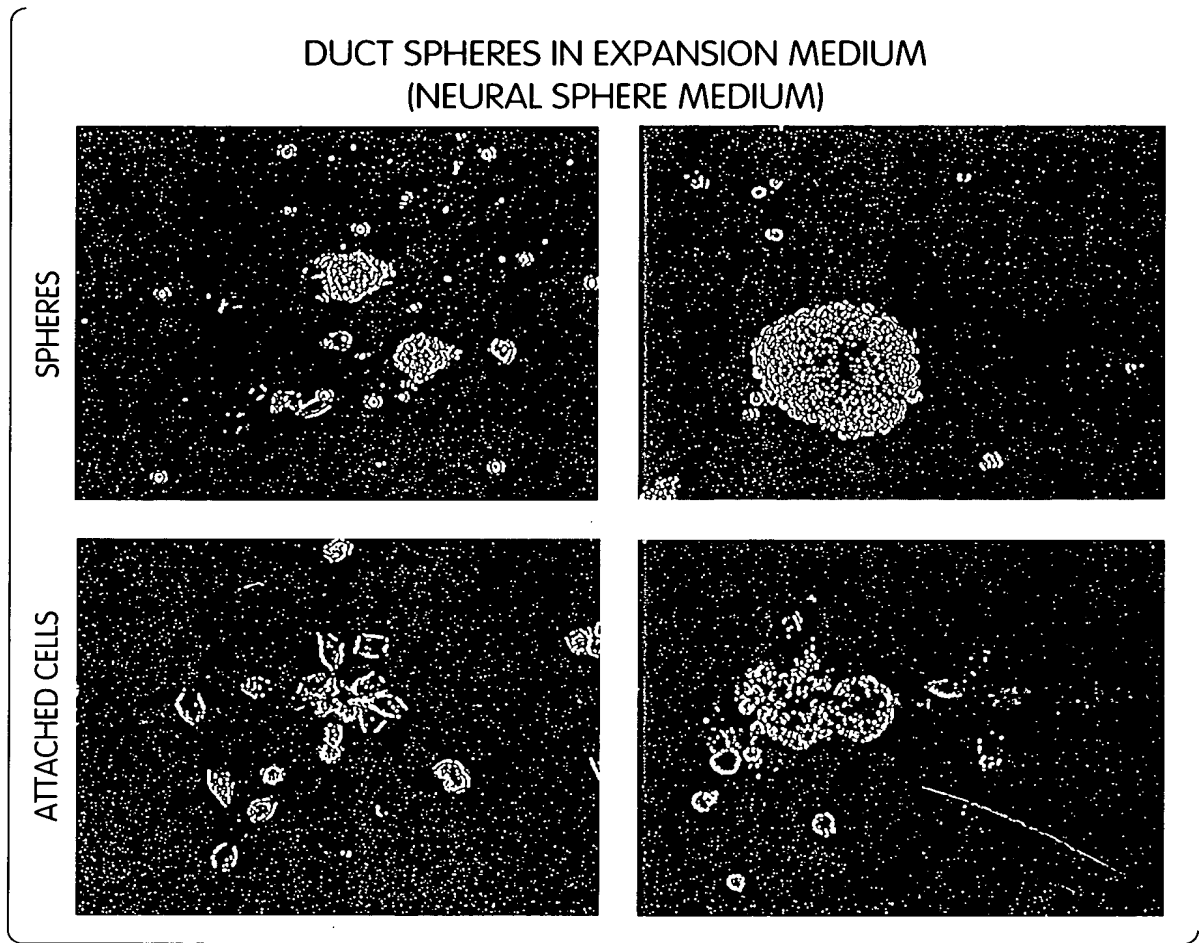
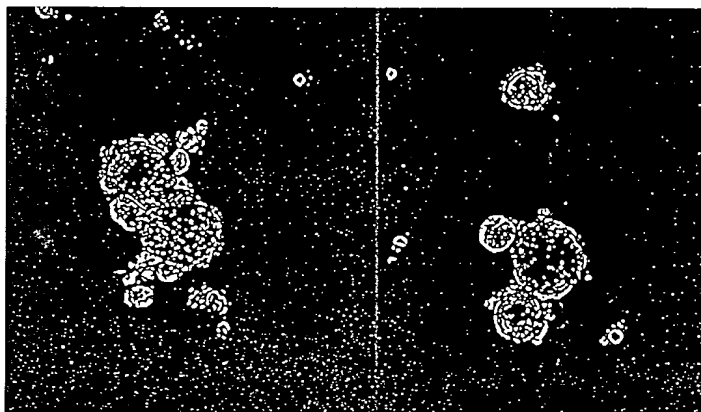


Fig. 41

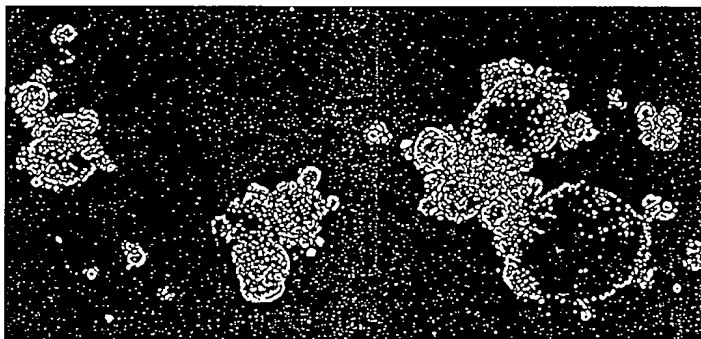
p14 DUCT PREP GROWN IN SPHERE MEDIA  
ON NON-TC SURFACE, p3  
ALL 10x mag.

MEDIA 1  
KO-B  
+15% KO-SR  
+TGF $\alpha$  + HGF  
+ IGF-I&II  
2mM GLUCOSE



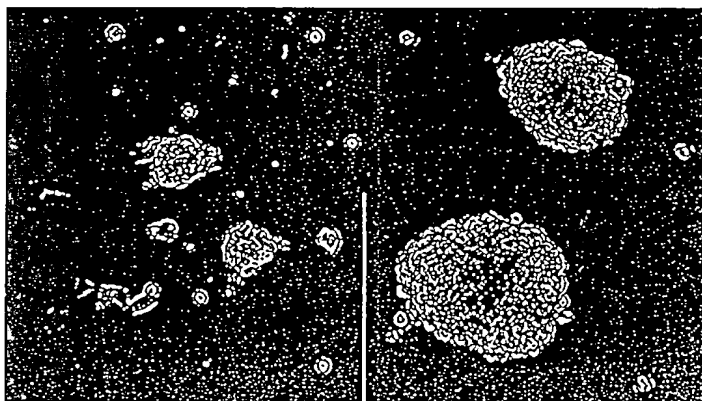
SLOWER GROWTH  
FEWER SPHERES  
HEALTHY

MEDIA 3  
LIVER BASAL  
+15% KO-SR  
+TGF $\alpha$  + HGF  
+ IGF-I&II  
11mM GLUCOSE



VERY FAST GROWTH  
MANY SPHERES  
LESS HEALTHY

NEUROSPHERE  
MEDIUM  
+Ins + EGF  
+bFGF + LIF  
17mM GLUCOSE



VERY HEALTHY  
VERY SLOW GROWTH  
FEW SPHERES

Fig. 42

DUCT SPHERE CELL *IN VITRO* DIFFERENTIATION  
- Glut2 / NESTIN

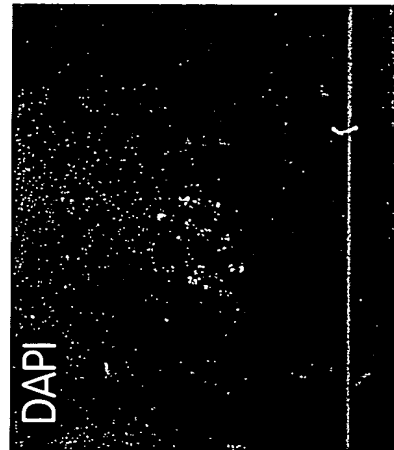
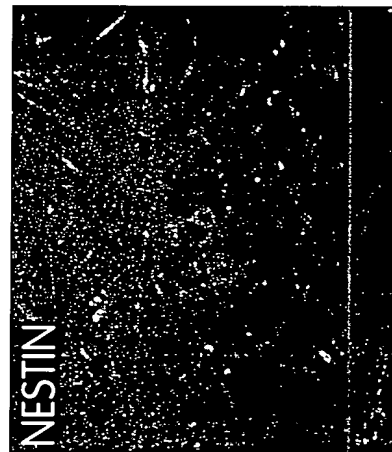
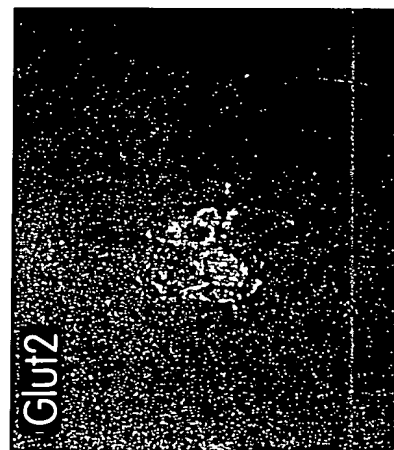
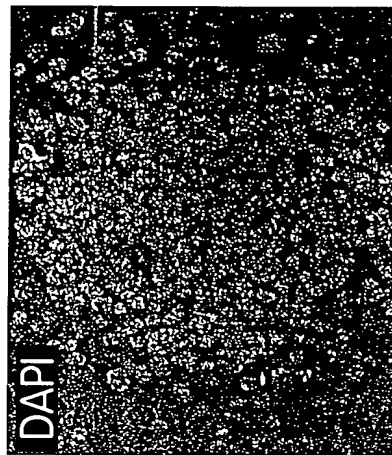
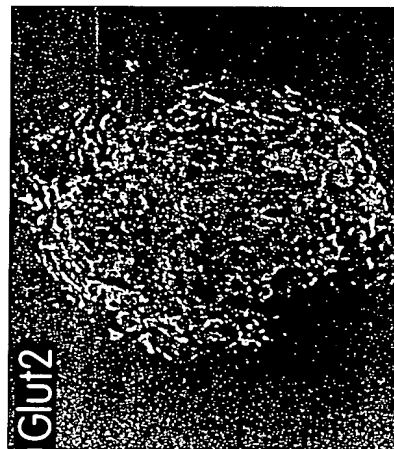
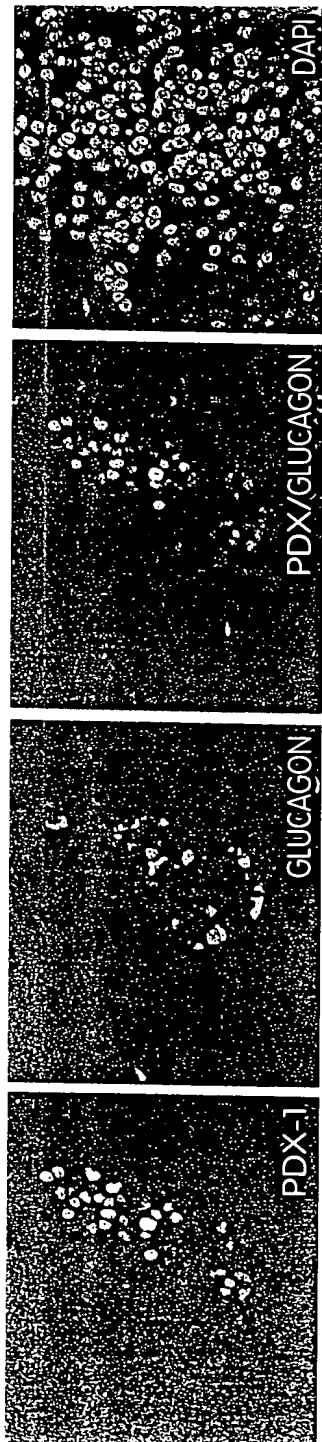


Fig. 43



DUCT SPHERE CELL IN VITRO DIFFERENTIATION  
- PDX / GLUCAGON

SINGLE CLUSTER



TWO CLUSTERS

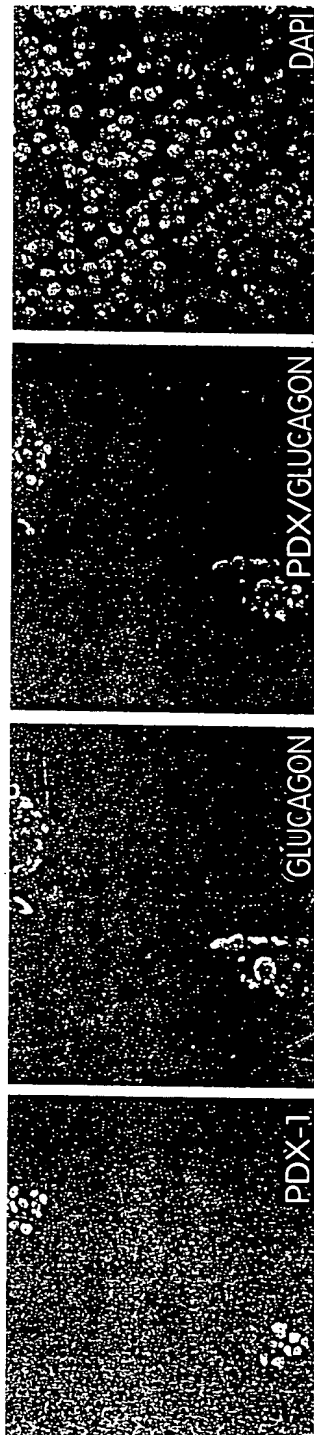
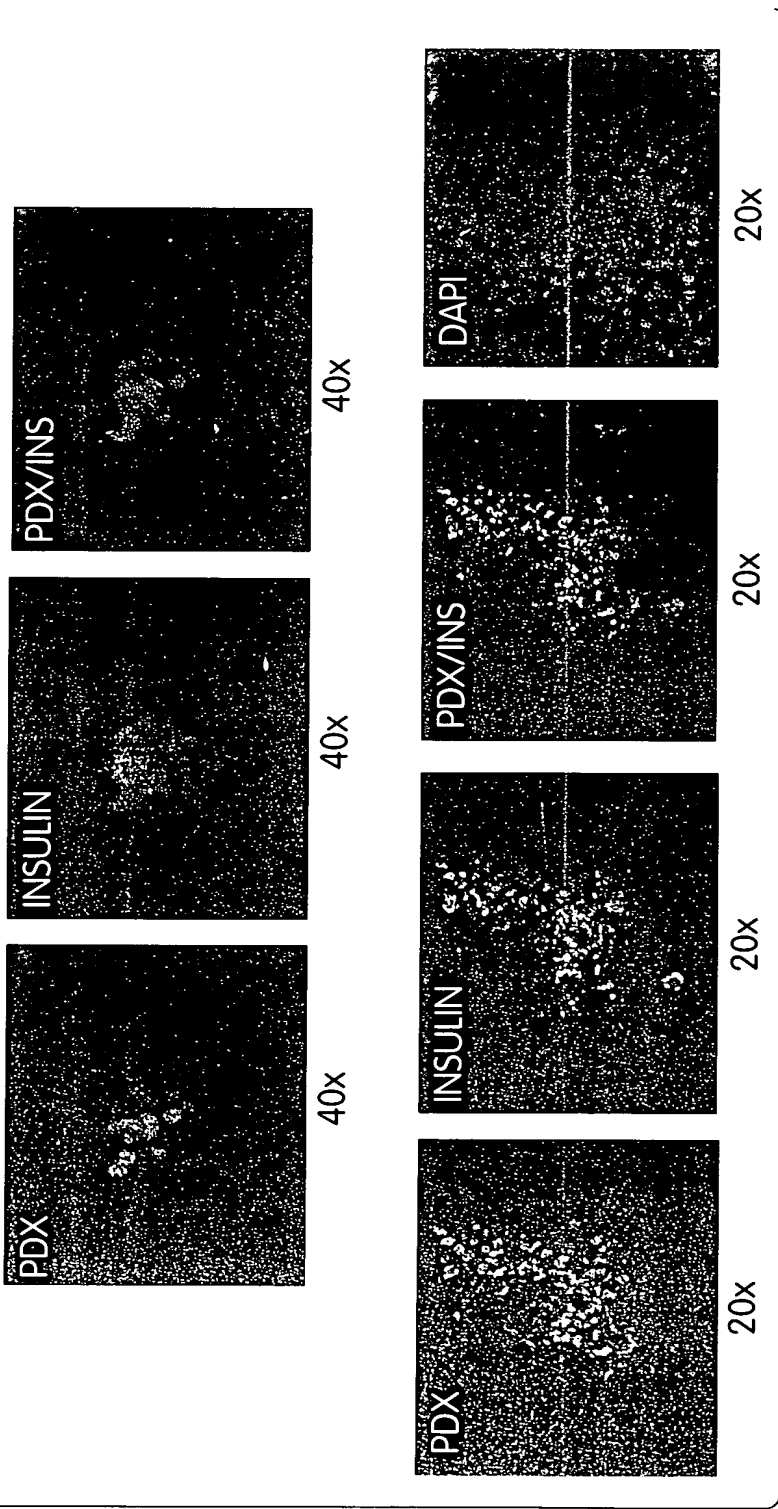


Fig. 44

DUCT SPHERE CELL *IN VITRO* DIFFERENTIATION  
- PDX / INSULIN





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### INSULIN POSITIVE CELLS IN PRIMARY DUCT SPHERES DURING GROWTH AND DIFFERENTIATION IN VITRO

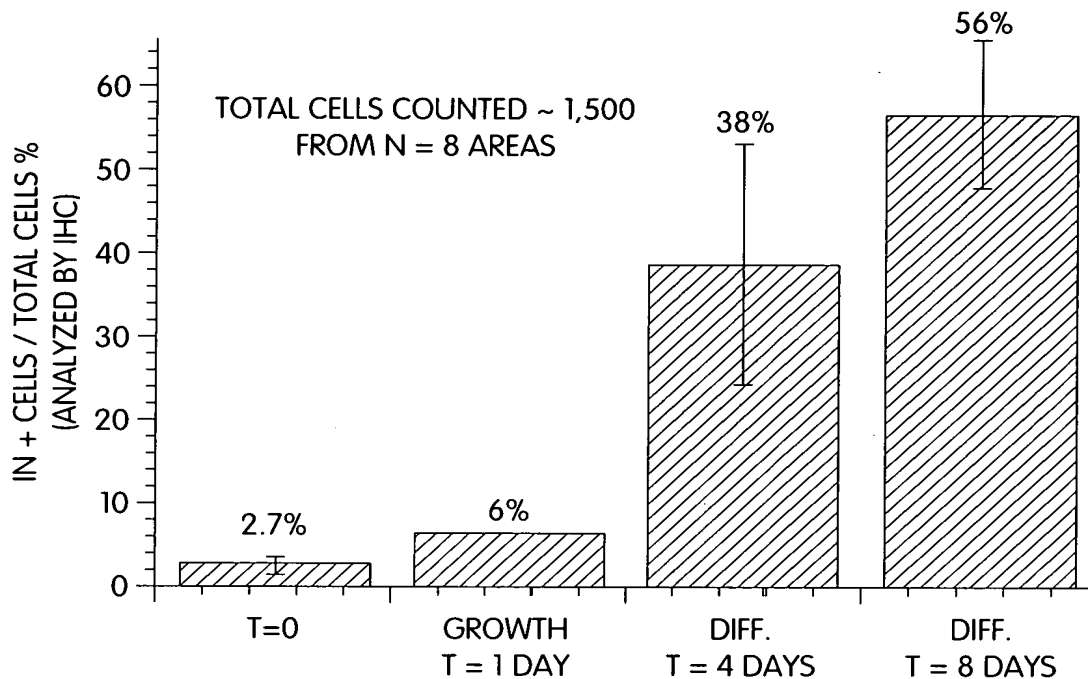


Fig. 46A

### Glut-2 AND IN POSITIVE CELLS IN PRIMARY SPHERE DURING GROWTH & DIFFERENTIATION

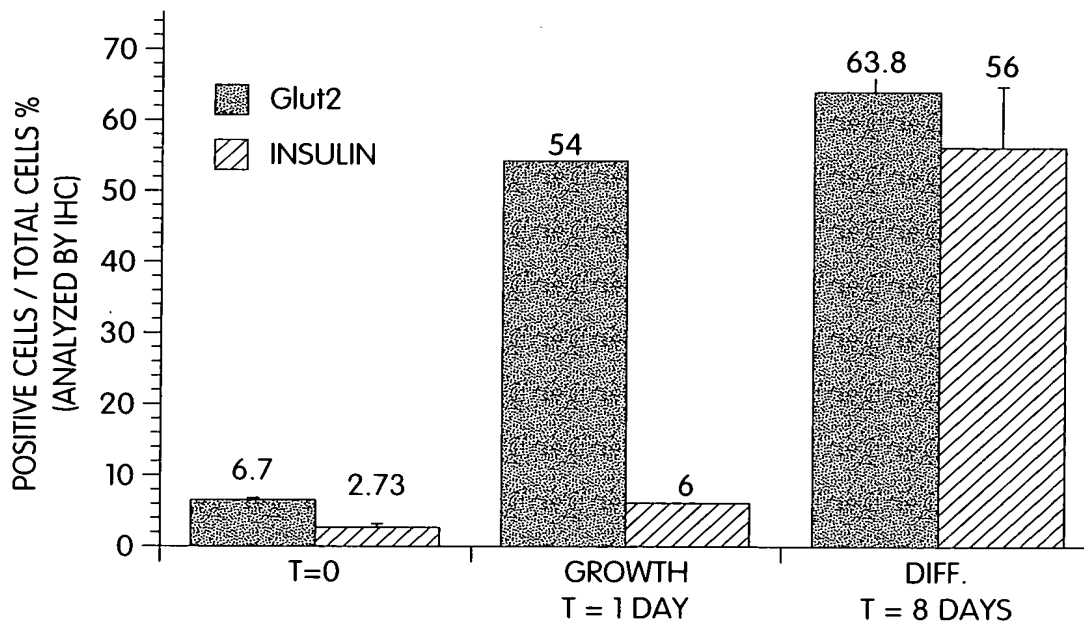
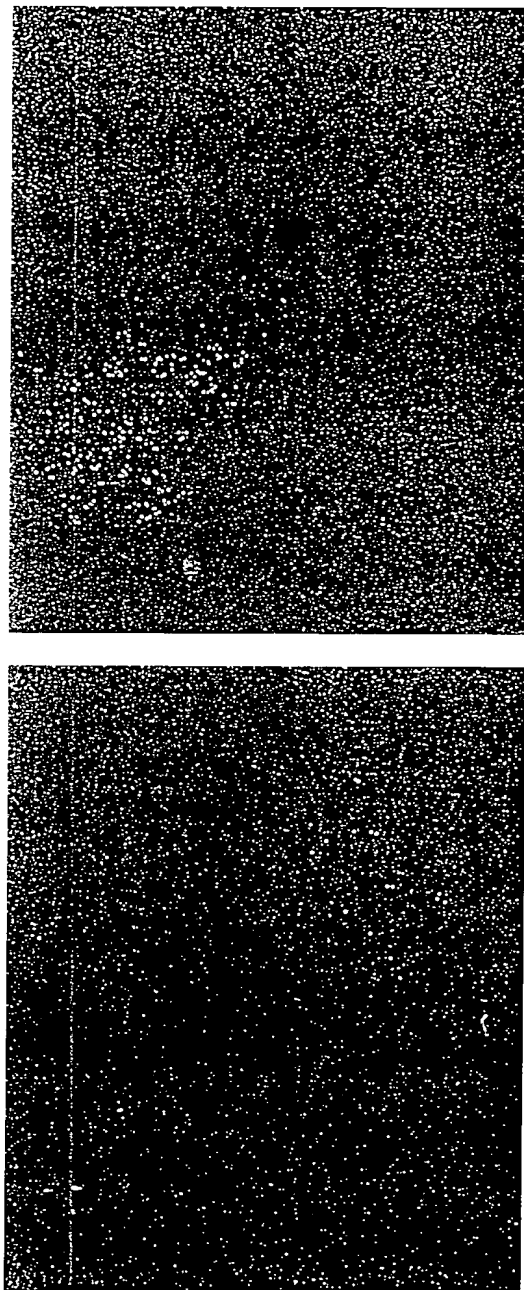


Fig. 46B

5.19 SPHERES ON CYTOSPIN SLIDE  
(SPHERE IN CULTURE FOR 24 DAYS)

NESTIN

DAPI



NESTIN/DAPI

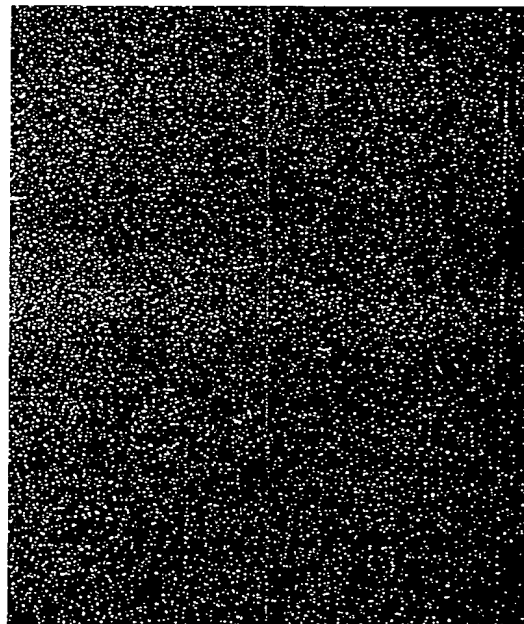


Fig. 47



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TABLE 1: MARKER STAINING IN 5.19-SPHERES ON CYTOSPIN  
SLIDES (UNDIFFERENTIATED CELLS)

(SPHERE IN CULTURE FOR 24 DAYS)

<u>MARKERS</u>	<u>POSITIVE CELLS/TOTAL CELLS</u>	<u>Ave:</u>
Pdx+	20/627 16/520 10/366 3/493	2.2 +/- 0.4%
IN+	10/627 8/520 6/366 3/493	0.11 +/- 0.03%
pdx/IN		60%
glut2+	5/562 6/495 2/503	0.82 +/- 0.03%
Nestin+	314/562 222/495 250/503	52 +/- 3.2%
glut2/nestin		0

Fig. 48



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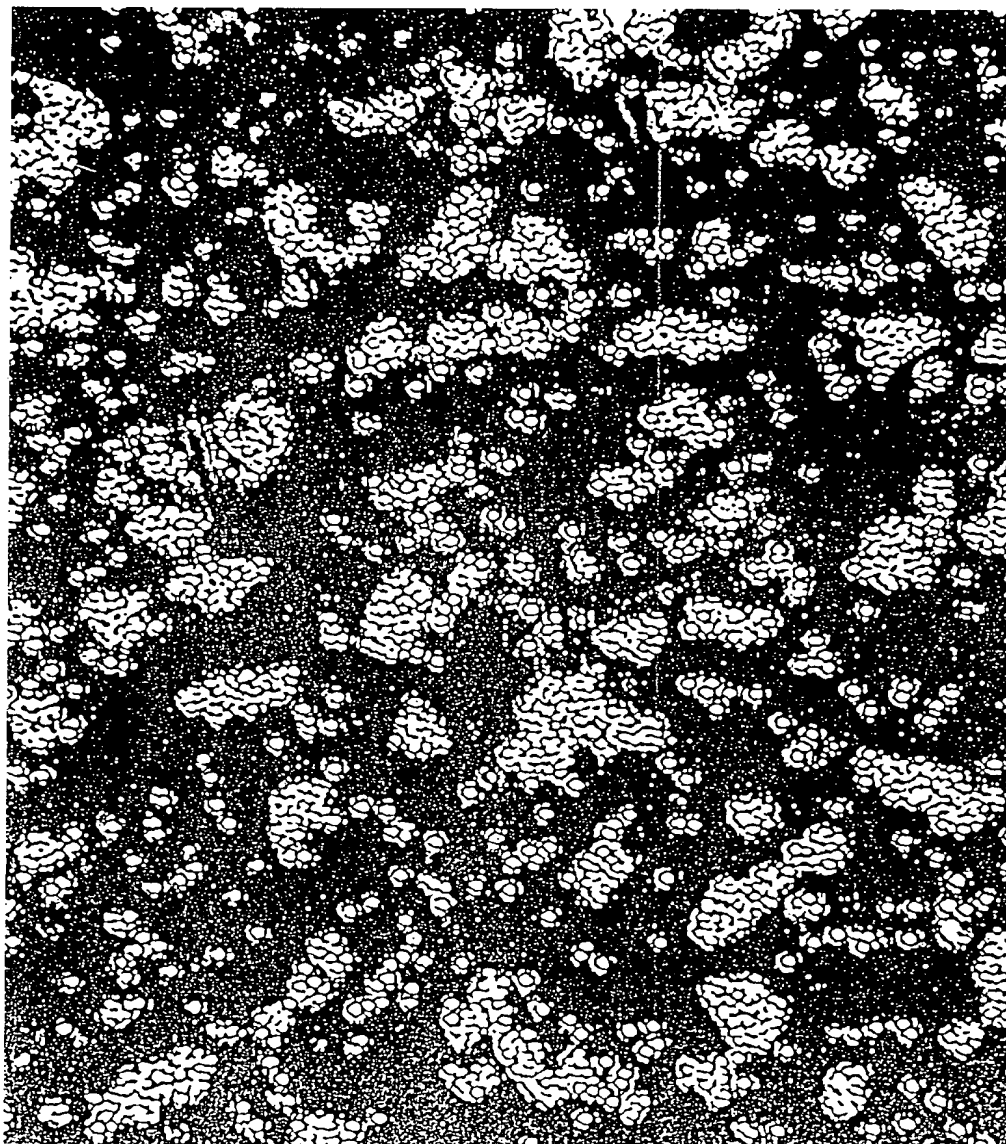


Fig. 49



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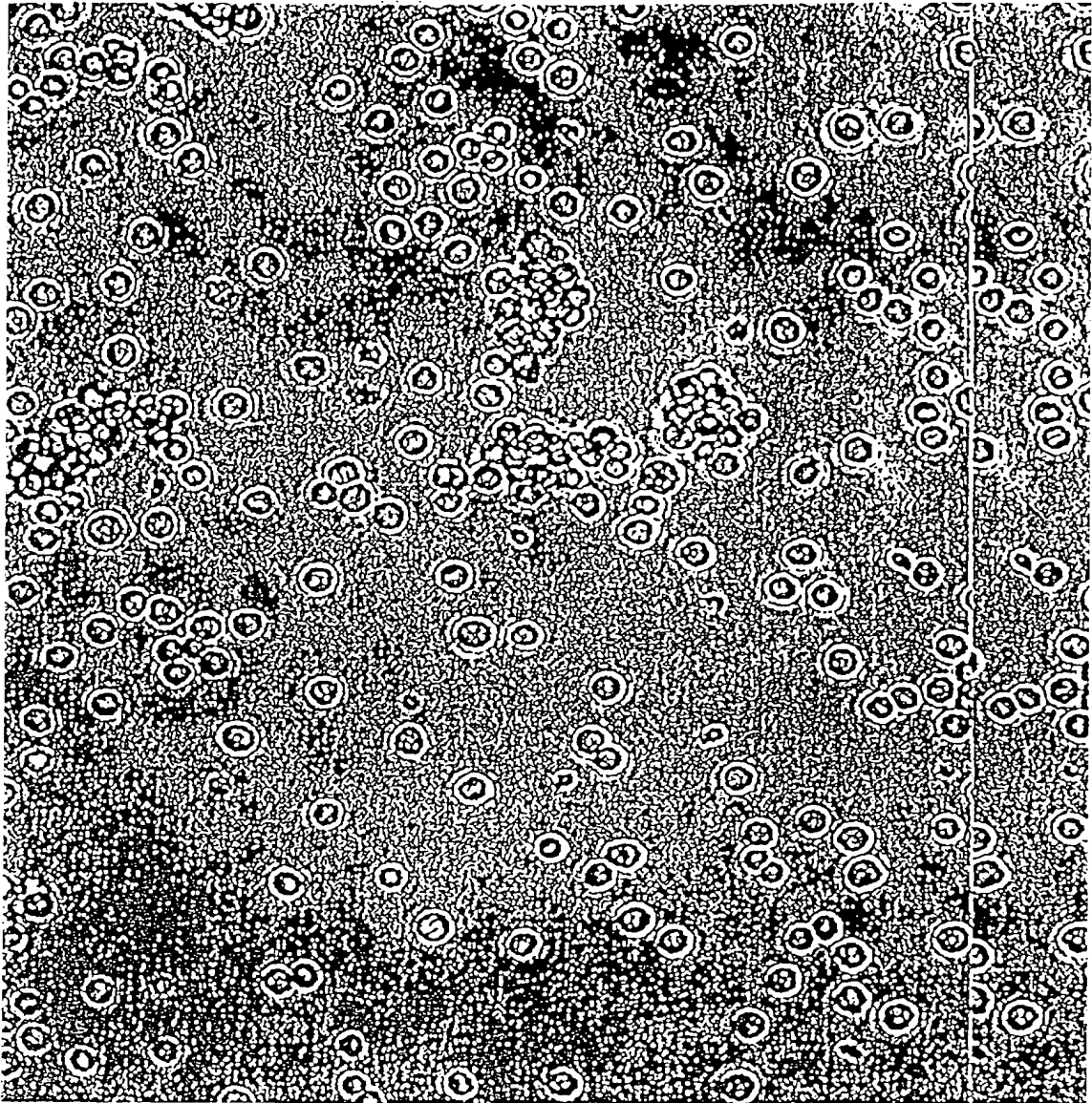


Fig. 50



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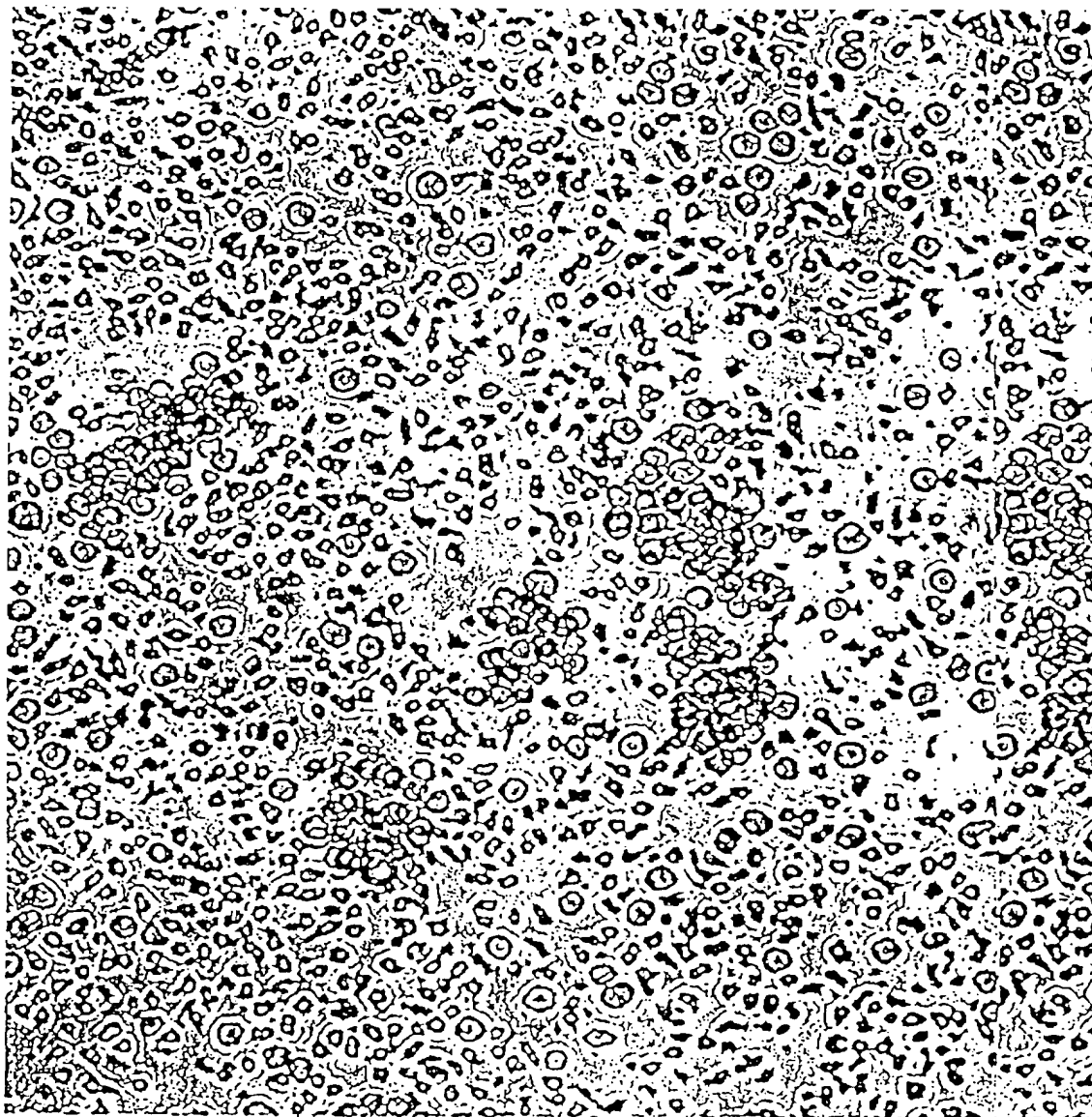


Fig. 51





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# STARTING POPULATION

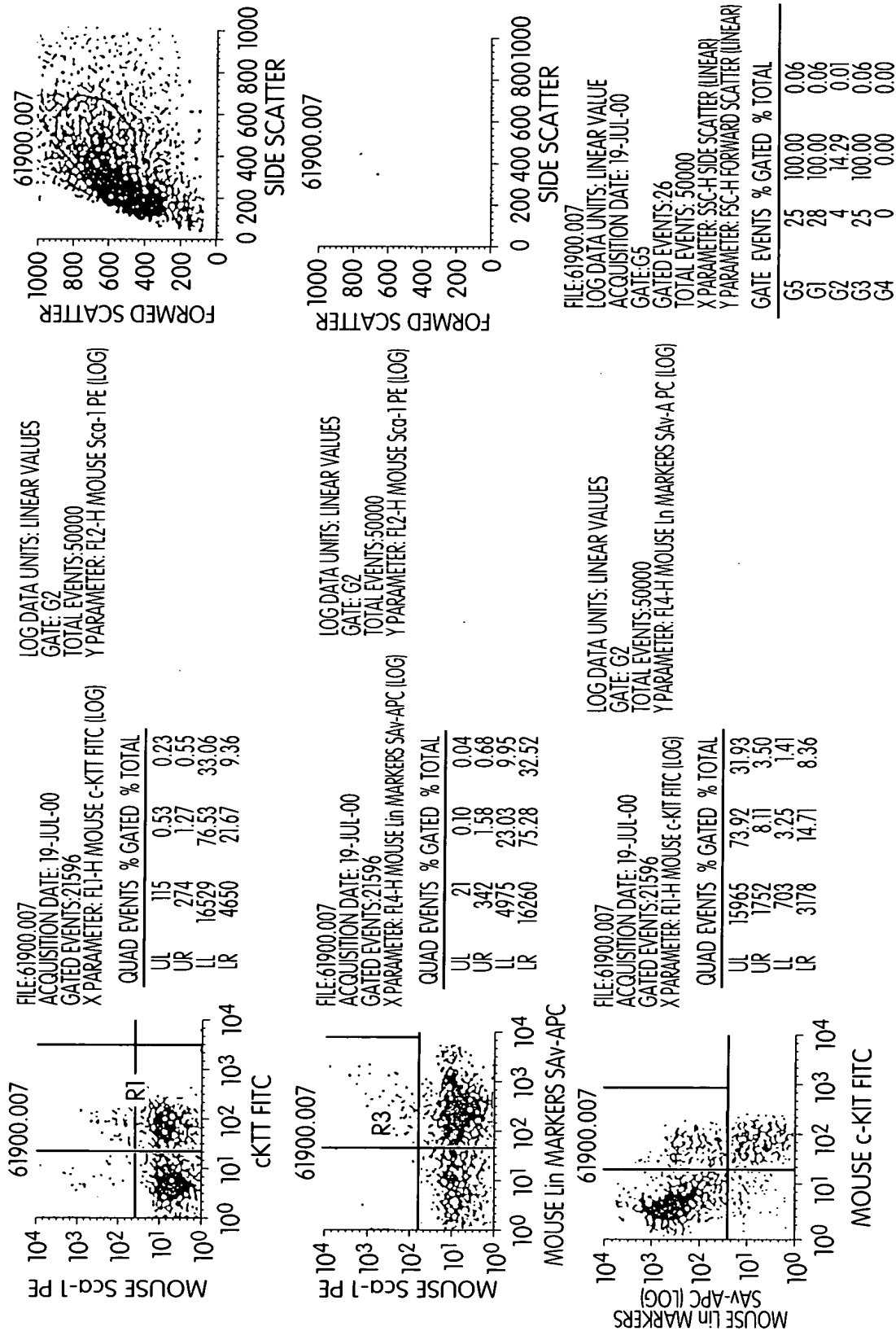


Fig. 52



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### AFTER LINT DEPLETION

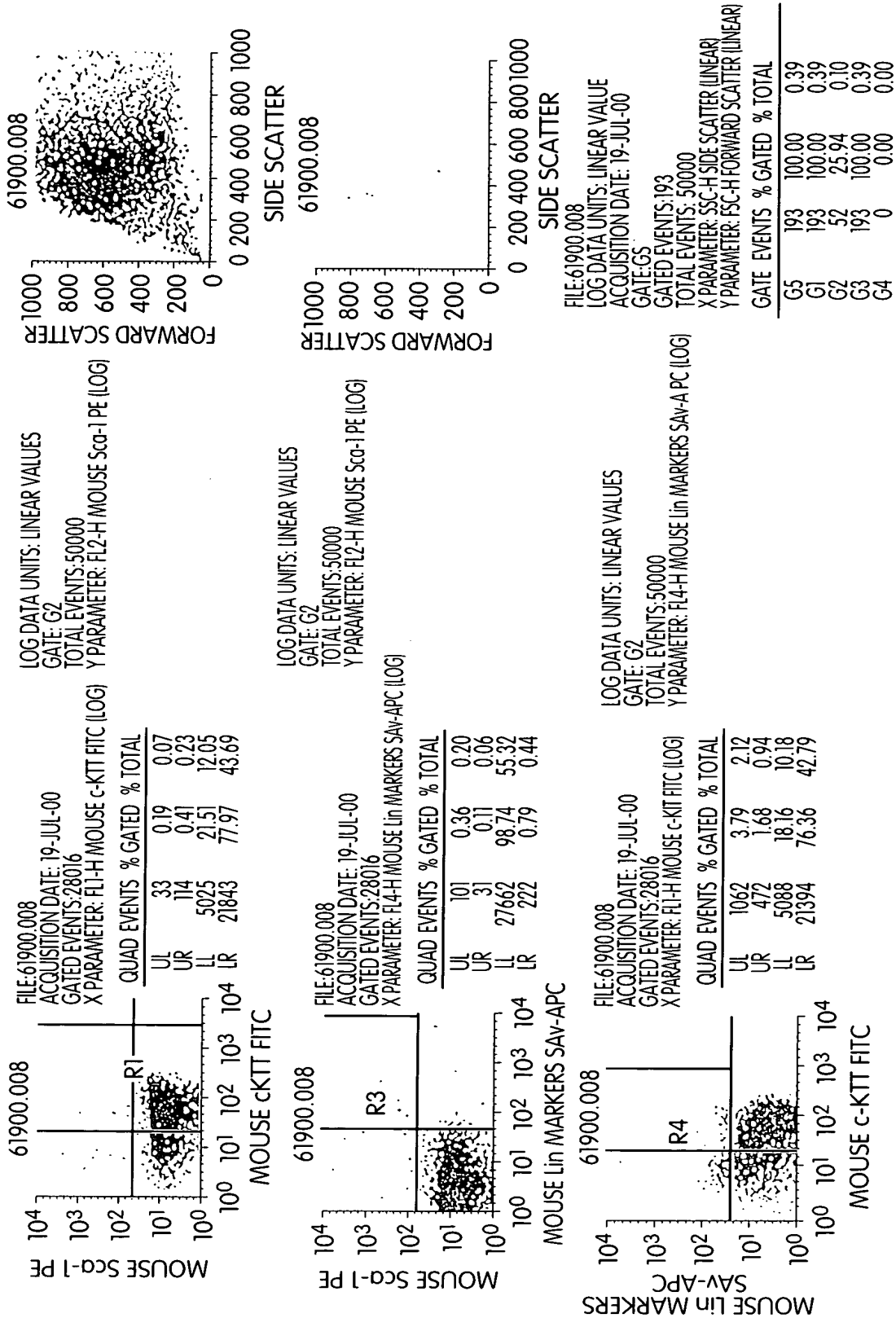


Fig. 53



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# AFTER 14 DAYS IN CULTURE

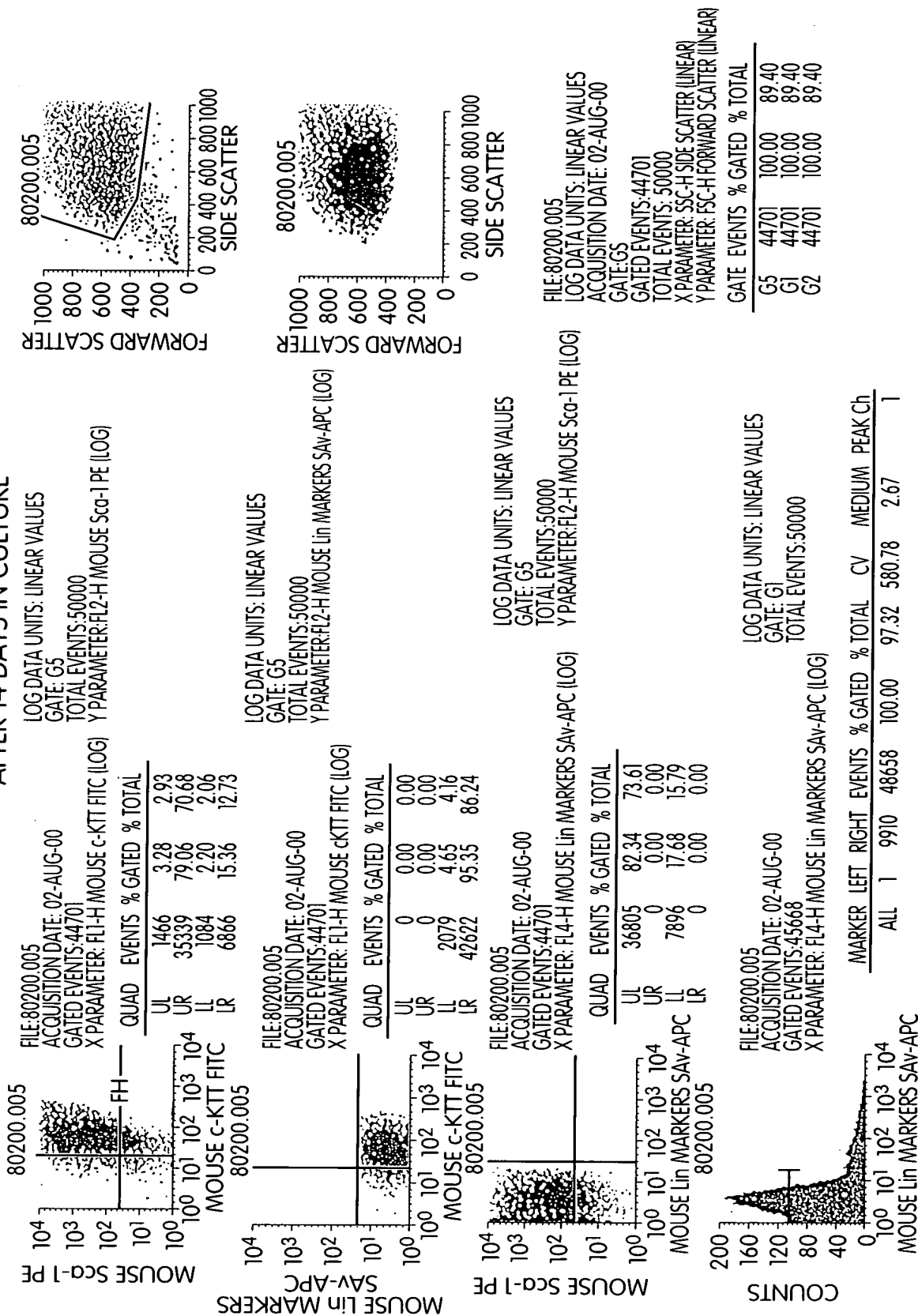


Fig. 54

# AFTER 20 DAYS IN CULTURE

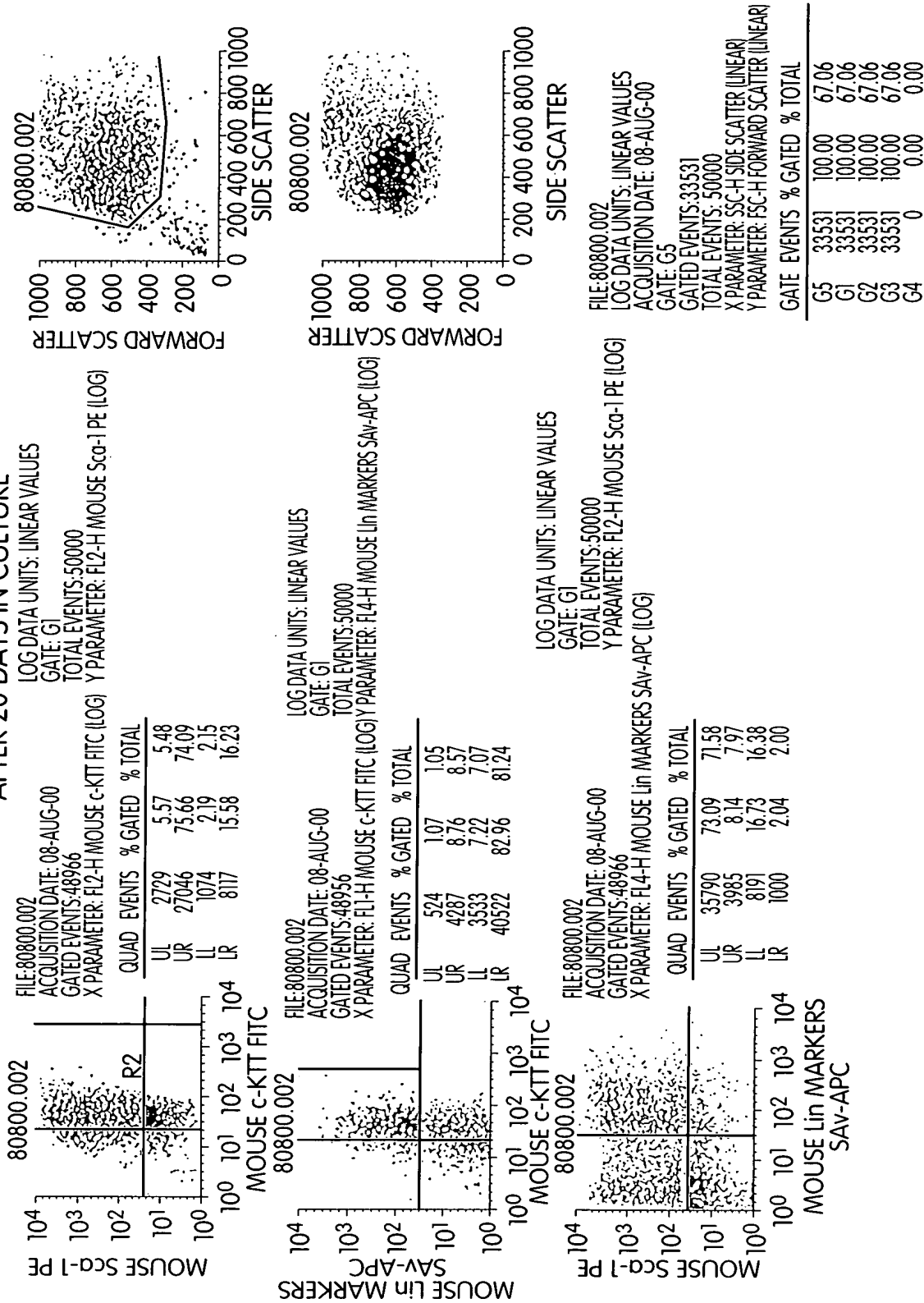


Fig. 55

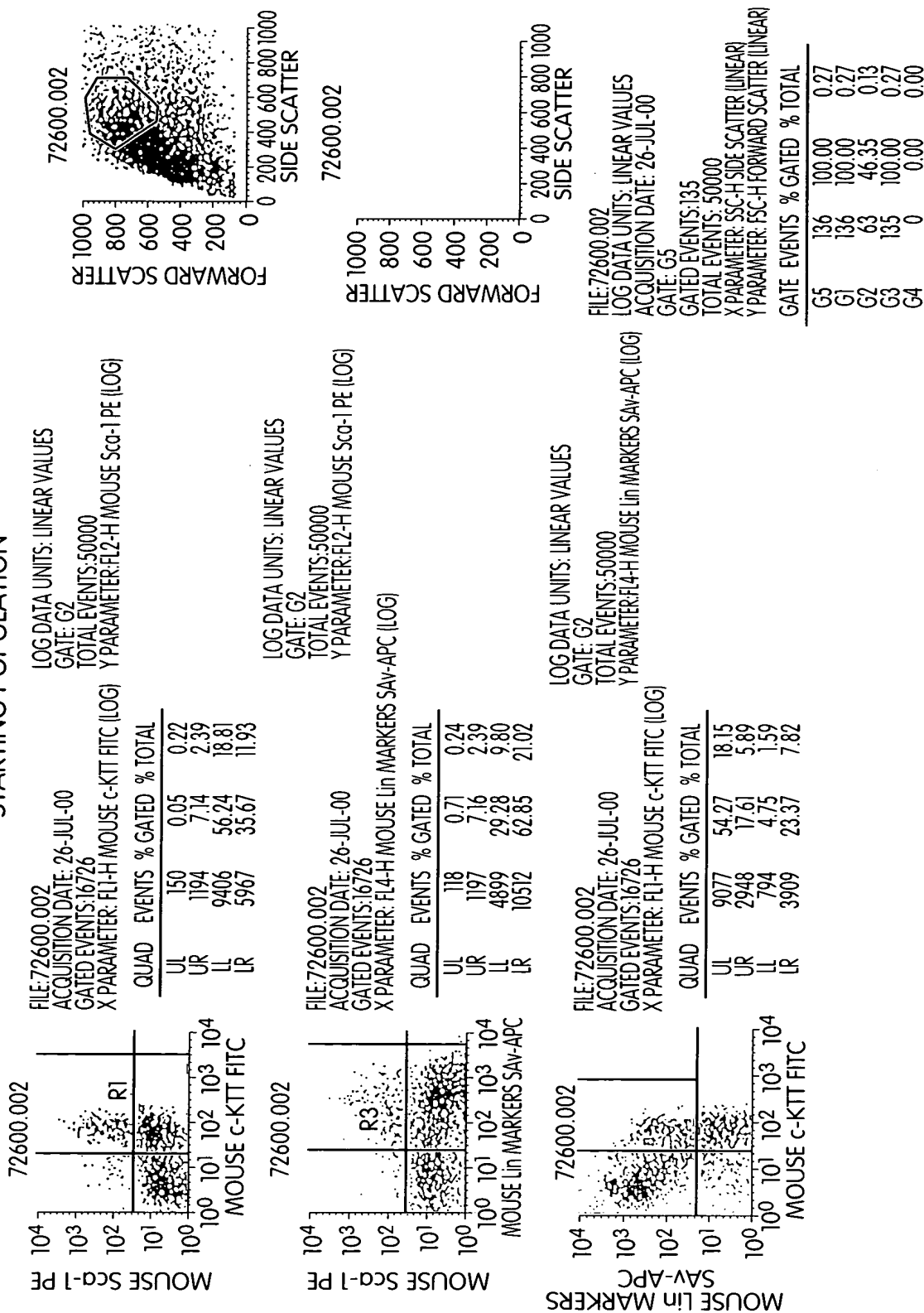
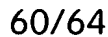


Fig. 56



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## AFTER LINT DEPLETION

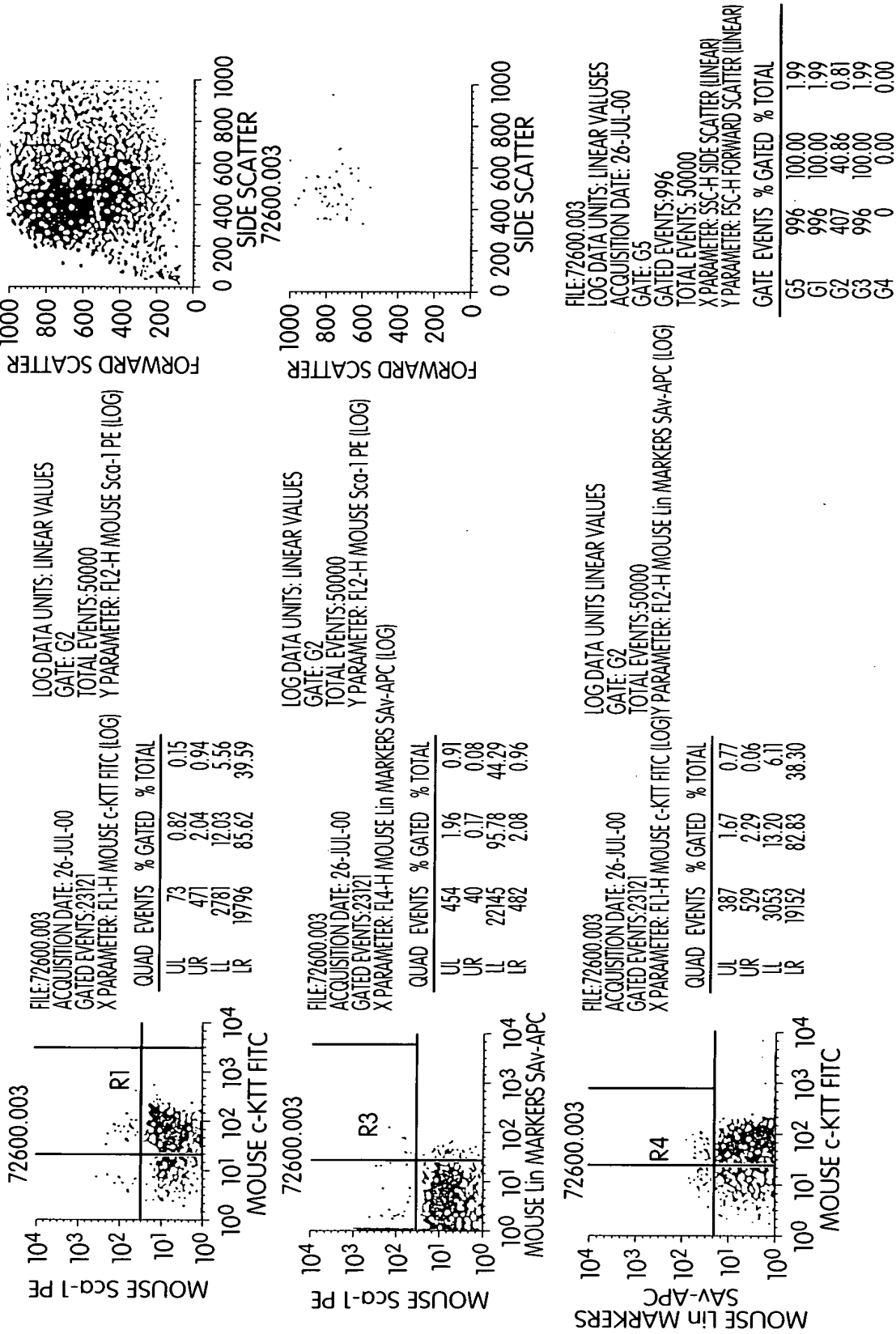


Fig. 57

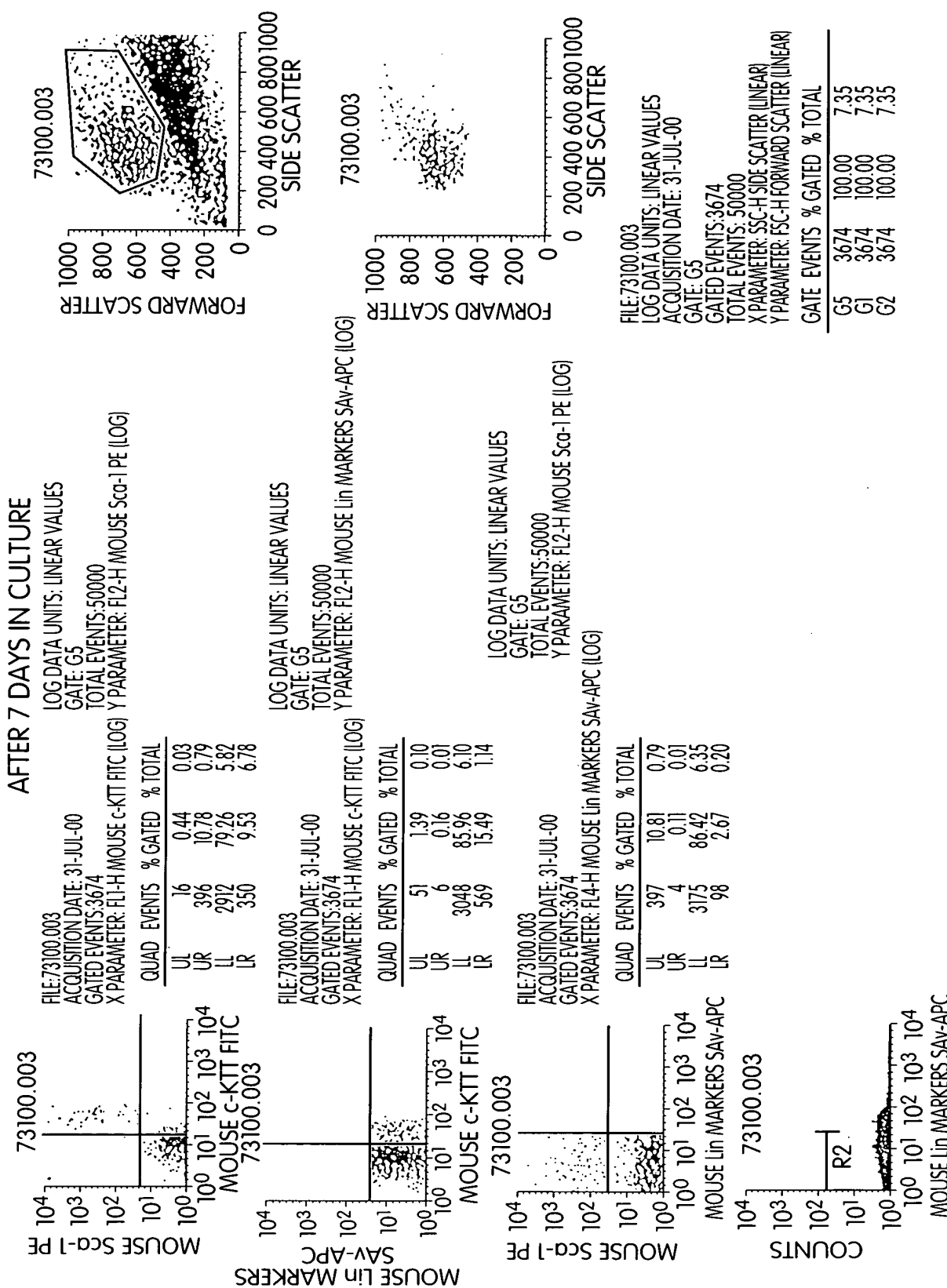
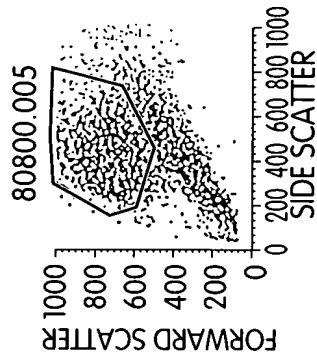


Fig. 58

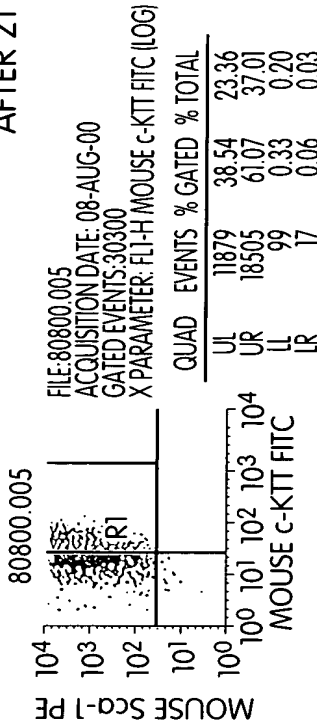


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### AFTER 21 DAYS IN CULTURE



LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS: 50000  
Y PARAMETER: FL2-H MOUSE Sca-1 PE (LOG)



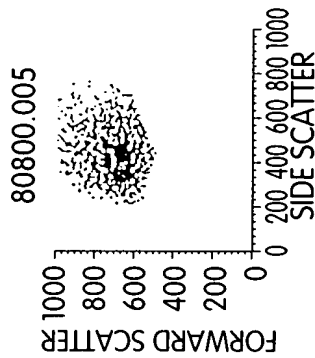
FILE:80800.005

ACQUISITION DATE: 08-AUG-00

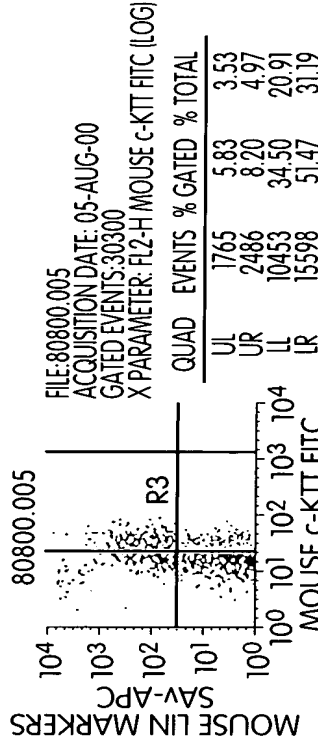
GATED EVENTS: 30300

X PARAMETER: FL1-H MOUSE c-KIT FITC (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	11879	38.54	23.36
UR	18505	61.07	37.01
LL	99	0.33	0.20
LR	17	0.06	0.03



LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS: 50000  
Y PARAMETER: FL4-H MOUSE Lin MARKERS SAV-APC (LOG)



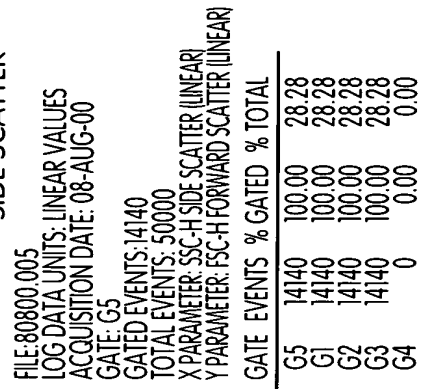
FILE:80800.005

ACQUISITION DATE: 05-AUG-00

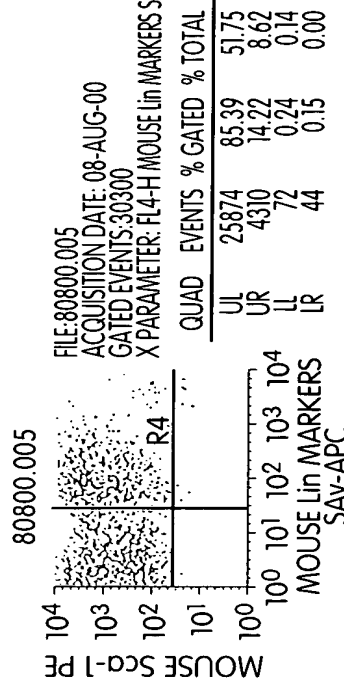
GATED EVENTS: 30300

X PARAMETER: FL2-H MOUSE c-KIT FITC (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	1765	5.83	3.33
UR	2486	8.20	4.97
LL	10453	34.50	20.91
LR	15598	51.47	31.19



LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS: 50000  
Y PARAMETER: FL2-H MOUSE Sca-1 PE (LOG)



FILE:80800.005

ACQUISITION DATE: 08-AUG-00

GATED EVENTS: 30300

X PARAMETER: FL4-H MOUSE Lin MARKERS SAV-APC (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	25874	85.39	51.75
UR	4310	14.22	8.62
LL	72	0.24	0.14
LR	44	0.15	0.00

Fig. 59





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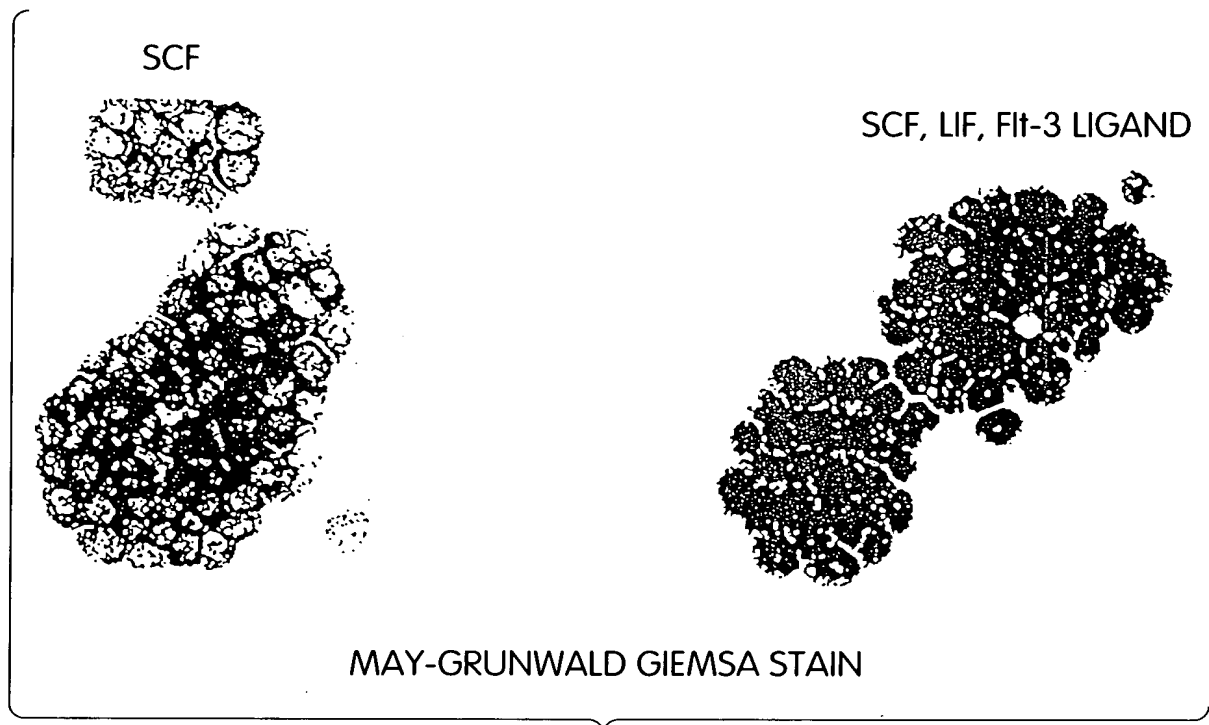


Fig. 60